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HUMAN ASPECTS OF SCIENTIFIC RESEARCH

By DR. WILLIAM A. HAMOR

MELLON INSTITUTE, PITTSBURGH, PA.

CONSPICUOUS throughout the world of to-day is the great diversity of science, which has been accomplished by the wide extension of the frontiers of knowledge of man and nature by the application of research. This research may be looked upon as the scientific quest for the possible. More precisely, it finds, observes, defines and applies positive facts by experimental methods and inductive logic. Research has characterized the life of the universities, which are primarily responsible for its existence. Having comprehended the spirit and power of research from the universities, the industries have utilized its methods in their own affairs with most beneficial results.

It seems that wherever research is alive it grows. The past thirty-five years have seen the number of industrial research laboratories in this country increase from a few to more than 3,000. But, without the evolution of scientific investigation in the universities, these industrial laboratories might never have been established. In addition to the very idea of research the universities have supplied the industries with men and women possessing knowledge not only of the underlying scientific facts and theories but of the methods and techniques of investigation. From the universities also has come much of the basic knowledge of science on which modern technology has been erected and will build in the future. The practical uses of science may be regarded as the dividends declared every once in a while by pure research and research education. When such research and education are hindered these dividends

must often be paid out of surplus and in a disaster such as war they may have to be taken from capital.

During the past several years the loss of science students and teachers and the assignment of remaining scientific personnel to wartime tasks have all but stopped pure research in our universities. The situation resulting from this expenditure of basic resources is so very serious that years of zealous effort in and for our research training schools will be required to provide an adequate supply of scientists and to put pure investigation on a prewar level. The Federal Government and our industries have been amply notified by the interested professions that pure research has waned and must be revived, that almost a generation of scientists has already been lost, that there will be a shortage of research personnel in the afterwar period, and that capable science teachers and fundamental research specialists should be returned to the universities. Let us trust there shall never again be a lapse in the continuity of pure research and research education. We must retrace our impressions of them upon the ground of hope for a long peace.

Reconstruction by Science

Researchful scientists in general perceive the importance to them of those considerations of the presuppositions of knowledge or of the general features of reality that are within the domain of philosophy. For that reason the philosophical principles of management have been infused into advanced research administration. There is wanting, however, a present-day view of science as a totality and there has been slow advance toward a philosophy of science which would bring about such a systematic whole.

Scientific education and investigation, with unavoidable increasing subdivision, would become more satisfactory as means of human progress by linkage with a broad survey of very complex science in its entirety. Some day there may be evolved a working philosophy to enrich the study of the past and present of science for the sake of the future, to illuminate scientific knowledge and its application to human problems. Then scientists could be successful in composing a synthesis in which all the sciences would be put in correct relation to one another, so that the field in which each research man is located would appear to him, not as an isolated region, but as a part of an aggregate, the general outlines and interconnections of which would be clear to every scientific worker and student. A layman could thereby grasp the ample implications and effects of a science, and hence the synthesis would facilitate the helpful absorption of fundamental scientific axioms in the wider domain of life. In applied science, service should be expressible in terms of sociologic and economic forecasting. The policies, conditions and methods conducing to communal well-being should be appraisable by scientific measurement. The demands for scientific research in bettering human relations in general will be discussed in the last section of this article following the consideration of basic phases of research management.

We are looking forward to a reconstructive world in which scientific investigation will give scope to the energizing impulse and to the shaping imagination. The value of research lies in its productive contributions to society. As the basis of solid managemental activity, it is fundamental to intelligent prediction, necessary to the verification of prevision. In investigational undertakings the scientific mind stays open and keeps eager: the scientist sinks himself in his problem, which becomes his essential life; his movement of self is from within outward, toward engrossment in an objective of human value. Such a scientist is engaged in doing something of societal utility that is the source of pride in his project; he is responsible to humanity being served. Research no less than education salvages potential human waste.

Philosophy of Research Management

Satisfying research management has for its goal the transformation of relations in ways that the finest and most effectual powers are evoked. Like all management of good substance it is never impersonal. It prevents loss of talent; it discovers just where persons best fit; it finds out how individuals can be better adapted to the work they do; it respects and protects professional freedom; it gives proper recognition.

Research management is concerned with precision and economy; its actions correspond to the facts sought. This management gives scientists opportunities to make their interests felt; it is therefore conservative of such interests. These scientists adhere to a functional unity of which they are a part, to which they are contributing. The functional laboratory organization renders supervision more easy by reconciling it with individual autonomy. The best organizer of arrangements for handling administrative matters on their proper levels is a generalist who knows how to use specialists and to keep them happy. Research is an adventure in cooperation by scientists who are always in earnest, and effective teamwork is facilitated by good-will, companionability and understanding of objective and parts to be played. The relations in research must rest upon mutuality and equality of privilege. Taking a common interest in the same things leads to united efforts. Response is both observed and anticipated, and it is developed by nurturing contented attitudes.

Persons who are kept in a state of good morale not readily lose interest in what they are doing. research man may be a small part of a laboratory; t if he has the right qualities, the right direction, right environment, the laboratory will be a great rt of him. Morale is personal in origin, operating om the top down. Only enlightened friendly and nest leadership in action can generate and sustain e esprit de corps that distinguishes the happy, isk, continuously advancing organization. The bet- rment of employee relations should be the joint ork of all executives, and management should con- antly point up every group activity until it actually romotes comity. Substantial change in personnel, pecially when suddenly effected, has often been en to affect morale and particularly to damage icely balanced working arrangements within an rganization.

A practical philosophy is the conception on our art of what is basically demanded of us. That hilosophy is discoverable in the animating idea of enterprise, in the unity of doctrine and spirit in erms of which all functions are performed, all details rganized—the principles that set the pace and di- ection. In reaching a philosophy every organiza- on must be perfectly straight and clear about its uiding concepts. After trial and success the true anagemental pattern becomes known and the phi- osophy is definable. Science uncovers facts through nvestigation and then describes them. Philosophical esearch management desires that its knowledge have seful meaning, that the significance and worth of actual information be found out. This manage- ent which thus requires perspective and valuation, xpects discoveries that have relation to the organi- ation, its purposes and boundaries. An integrative esearch philosophy has regard for the logic of vents, emotions and sentiments; it communicates ent of mind; it conduces to personal as well as rganizational advancement.

Public and Professional Relations of a Research Institution

The health of a research institution depends upon he maintenance of a correct balance among four omponents: staff life, systematic pursuit of new nowledge, teaching of high professional ideals and rovision of support for the activities, both internal nd external. Where such an organization has pur- poses not involving pecuniary profit, societally valu- able results are always planned to accrue. The ernel of non-profit is proportionality—nothing in xcess in motives, everything in the right connection, properly balanced for public benefit. The aim is ot to make money, only to give as excellent pro- fessional service as possible.

Having gained respect through managemental and investigational accomplishments, a research institution can extend its scientific activities into other fields. It can aid in showing the high importance of depending upon facts. It can assist in popularizing scientific research by demonstrating its usefulness through the media of addresses, press releases and literature. It can help in planning for peacetime public and professional satisfaction. It can exalt pure research. The public as well as the industries will have faith in the utility of the scientific method when that value is proved again and again. A cardinal principle is that a research institution should concentrate on long-range basic problems, on preventive and constructive programs that do not displace projects of other kinds of organization. A research institution should supplement other establishments in its field and should have a part in stimulating scientific effort everywhere in that province. The increasing growth of research puts a high premium on the improvement of professional relations among institutions, consultants and commercial laboratories.

A research institution often receives appeals for counsel from companies that want technical assistance. Most of these requests relate to scientific or managemental questions that generally can be either answered at once or referred to consulting firms. By this channel an institution can cooperate with other research establishments or professional practitioners. Sometimes, however, it will be learned that manufacturers need research specialists in their organizations; therefore they can be encouraged and assisted in finding properly qualified persons.

Coming Changes in Research Relations

In the afterwar period there will be new problems in regard to research workers. Scientists and engineers who are in the armed services or who have left laboratories to assume some other class of temporary civilian employment will have adjustments to make when they return, and both they and many persons who have been in essential research through the war period are wondering about where and how they will fit into the future. Numerous young men of science and engineering have gained mental development, have shown new abilities in military duties. The shift from the stage of wartime pressures and tensions to a transitional or peacetime era will surely require mutation in attitudes as well as in formal managemental policies and organization.

History has repeated itself, and procedures employed in military personnel activities are being proposed for use in peace. Indeed industrial management is studying war agency applications of psychology in the selection and classification of per-

sonnel, in the influence and measurement of attitudes and in intramural and extramural relations. In war there is occasion for the intense application of science to urgent problems; research is stripped of wishful thinking. It is therefore to be hoped the valuable methods and techniques will be adapted with discrimination. Both management and labor will have an attitude more favorable than in the prewar period for the use of scientific research and tools. The postwar period will likewise be entered with greater emphasis on the importance of human relations than we have known. There will be a rich heritage of information gained from science and from the application of research findings. During wartime, as has been brought out, research knowledge is used chiefly in pressing short-time studies. In peace long-range fundamental research has exhilarating surroundings it can not locate in the interruptions of conflict.

Industrial reconversion and re-employment are under way and will be accelerated as time goes on. Communities as well as companies are trying to find how they can gage the impact of the war, how they can get ready for shifts of production to peacetime requirements. The urgent necessity for reviving business in the postwar period is spurring many manufacturers, some of them for the first time, to improve their practices. Changes will be in the postwar air, and alert organizations are preparing for them. It seems certain that the strategy and tactics of industrial research and their bearing on national welfare will be much more essential several years hence from what they are to-day, that researches of wide scope will be in motion throughout the industries. The experience of the war will enlarge points of view, will expand responsibilities. Scientists and engineers from the martial services will become strong elements in reorganization and reconstruction after their return because of their knowledge of personnel relations, executive work and other military activities. They will be willing to face and to cope with arduous problems and will be sympathetic to intellectual adventure. They will help to make encouraging the outlook for satisfactory employment. We should not neglect searches for science talent in the armed forces, to facilitate the subsequent recruitment of promising personnel.

Professional societies, universities and research institutions can be of advisory aid to scientists and engineers, such as veterans, in coping with their readjustment and placement problems—in securing professional positions, temporary or part-time employment, retraining or graduate or post-doctoral grants. They can also give suggestive guidance to persons now or formerly in research who are unfitted for careers therein. Research personnel problems that lie ahead should be studied from all approache and corners. We must find out how and where w can best use men and women to their highest potentia in assuring the maximum of employment, productio and well-being.

Special Training for Research Service

As the accomplishments of men of research gro more and more prominent in every sphere of lif the security of society makes most important th sage and full utilization of their unusual assortmen of qualities and skills. The administration of re search ability will therefore increase in essentialit as will the obligation of developing new researc executives. We should constantly strive to encour age the desire for responsibility and to furnish train ing bases for scientists possessing evident funda mental qualifications for managerial posts. Th moulding and enlivening of any executive develop ment program require sound judgment and the man agemental guidance that has all-out concurrence- leadership possessing familiarity with the intricacie of human nature. We have under examination set of tests for selecting research executives. If ade quately validated later on, the procedure will b reported.

In particular we should give more and more at tention to the branch of management that treats o the personal and official duties of researchists, i distinction from the much better known subject o systematic research, which deals with literature studie and experimental methods. We should intensify th personal factor in all such professional work as w have ample evidence that this action contributes t individual and organizational happiness and succes and to friendships in and for science and its in vestigation. Research management should therefor endeavor to unfold and widen the interests of em ployees, to make easy their perception of the over-al significance of their life and obligations and of th value of personal audits at regular intervals, t encourage relations and activities necessary in bring ing about symmetrical personalities. In the per sonal enrichment of a scientist's life there is abov all involved the attainment of a liberal attitude, sympathy with human living, an understanding o the aspirations of others. Thus there can be culti vated those special kinds of discernment called sense of humor, judgment and proportion.

Laboratory personnel management has a weighty place in developing young men for commercial and public service, mainly because it can impart useful information, largely gleaned from the experience o industrial research administration, that is not acquired in scientific courses in the universities. Researc

staff members can be educated in managemental procedures in general, in the minutiae of professional ethics and relations, in the differentiation of people and things, of personnel and materiel and their connections, in economic principles and trade knowledge, and in the psychology of the industrial mind. Relative emphasis accorded to the last-mentioned subject will gradually enable a young scientist of correct attitude to appreciate the commercial standpoint. It will teach him to convey to the industrial or business executive the ideas of science and the results of research in a manner and language that can be easily understood. Informed genial conversation is one of the best features of well-rounded professional life. In industrial research, especially in practical associations with company officers, the art of making and keeping contact and of promoting polite, tactful and friendly relations is of constant utility. It is of great aid in gaining essential cooperation and in securing the confidence that springs primarily from research accomplishment and technical merit. All successful industrial research as well as all successful professional and public relations are built upon trust. Among the foremost agencies for advancing research and its votaries are the scientific societies with their coordination, conventions and publications.

Research Demands in Human Relations

Scientific research has manifold societal and personal facts. In industry, for example, it is confronted with problems relating to workers as representatives of complex society as well as with problems involving interactions of workers and managers as individuals. In another type of problem study is being given to the recognition of the limit, if one can be found, beyond which production and distribution are likely to disturb the areas of industrial management and communal life. Applied physical science has been a very revolutionary and constructive factor in the industries, but to economists and sociologists concerned with the stability of communities it is of perturbing influence. Natural scientists could be of much aid to them in investigating that variation broadly along with other dynamic problems of improving human relations.

If after the readvent of peace we could produce and market goods at the same rate as in wartime, we should have the highest standard of living ever experienced, provided we could rightly solve our human relations enigmas. Of necessity in attacking these difficult questions is the correct and full use of scientific methods. We also need faith as well as facts and therefore psychological and ethical standards must be determined. To cite an instance, let us take the objective of personnel management research, which is the improvement of the understanding of people, of quality of judgment, of employee effectiveness and contentment and of corresponding techniques. Just as research is essential to all technologic progress, so is it indispensable to the advancement of personnel relations.

Many studies have been made on human problems of the industries, embracing sectors of their labor and public relationships, and discoveries in natural science have been stimulating in influence in all portions of the work; but much investigation remains to be performed to bring satisfactory results. It must be borne in mind that the activities in human relations have been too largely casual, the knowledge and experimentation too inadequate, to be comparable with the facts and methods of natural science. What needs to be done is apparent in general; how it shall be accomplished requires elaborate attention. We do know, however, that progress in human relations is dependent upon sufficient and efficient research on the value of what we have taken for granted, on the tendency and usefulness of change, and on new means to meet advantageously the real conditions of living and working to-day and to-morrow. This research must be conducted and its results utilized wisely if we are to pass the bounds, the numerous unsolved human problems, that hedge about us, little affected by ready measures of control. With science as the afterwar societal architect we could gain an economy and accompanying standards of human relations that would encourage the good life and thereby help importantly in preserving peace.

The United Nations organization has the unprecedented opportunity to foster research on defining the cogent relations among state and human interests and the facts of current reality, with the objective of evolving scientific means for bettering national and worldwide human relationships. Such a powerful action would stimulate the revival of fundamental investigation and also education in the universities, would inspire the improvement of public, institutional and technologic life in the postwar era. It would help to prevent the adaptation of science to adverse social philosophy; it would instead encourage an intelligent demand for science in the societal field and the development of a generally acceptable philosophy of science; it would thereby strengthen the realizable usefulness of scientific research. The United Nations could thus extend the versatility and creativeness of science and research to their own peacetime administration and promotion of progress, so as to invigorate and safeguard all that rightfully belongs to them as political bodies and to man as man.

OBITUARY

DR. PETER I. WOLD AS PROFESSOR OF PHYSICS AT UNION COLLEGE 1920–1945

COMPARED to other physicists whom I have known, Dr. Peter I. Wold was fortunate in combining natural gifts with varied study and experience in academic teaching and administration in China and the United States as a crown to his practical work with government bureaus in Washington and long connection with the laboratory of the Western Electric Company. In 1920 at the age of thirty-nine, he became head of the Department of Physics of Union College that had suffered from past neglect during and after the first World War. To Dr. Wold could be applied what President Charles Eliot of Harvard said of one of his young professors, "A gentleman, and an able scholar, teacher and administrator." He had exuberant enthusiasm and robust health; a far-seeing vision for his ideal department of physics; abounding energy; a humanistic background and an ability to cooperate with his colleagues. This belief in the Biblical admonition of, "Ask, and it shall be given you; seek, and ye shall find" captured the imagination of the college trustees, especially Mr. E. W. Rice, Jr., and resulted in a new laboratory building, enlarged staff and an ever up-to-date curriculum. Dr. Wold possessed a rare ability to judge men for his staff, surrounding himself with brilliant, industrious and resourceful young scholars. For twenty-five years he labored with others to improve and integrate the whole curriculum for the bachelor of science degree, making it broad and comprehensive, yet giving scope for the training of specialists, by the inclusion of research for qualified students and leading to select graduate courses. The later success of his students tells the best story.

Dr. Wold had the gift of delivering scholarly and thrilling lectures adapted to the understanding of popular, even youthful, audiences, for he spiced his exposition with humorous asides, as he performed his mysterious experiments with the air of a skilful conjuror!

GEORGE DWIGHT KELLOGG

LAWRENCE JOHN PALMER

LAWRENCE JOHN PALMER, who died at Anchorage, Alaska, on June 20, 1945, was born to Axel R. and Laura Lundberg Palmer in Rockford, Illinois, on January 19, 1893. He was educated in the public schools of Illinois and at the University of Nebraska, where he received the B.S. degree in 1915. He was employed summers and after graduation in the Forest Service, in which organization he was assigned to grazing studies of which he was in charge in District 4 (Intermountain Region) in 1917–18. He then transferred to the Biological Survey to undertake reindeer grazing investigations in Alaska. He attained the rank of senior biologist in charge of the Reindeer Experiment Station at the Agricultural College of Alaska, 1928–36, returned to the Forest Service as principal forest ecologist at the Rocky Mountain Forest and Range Experiment Station, 1936–37, and again to the Biological Survey in 1937 as principal biologist in investigations of the wildlife resources of Alaska. In 1944 he transferred to the Office of Indian Affairs.

In the early 1920's, when the only means of travel in northwestern Alaska during the winter season was by dog and reindeer team, Palmer made a survey of reindeer herds all along the coast of Bering Sea from the Kuskokwim River to Kotzebue Sound. During this period he began the collection of lichens and other tundra plants that was to become one of the largest of its kind.

Palmer, a tireless field worker, was highly respected by the several factions that developed as a result of the white man's attempt to commercialize and build up an export trade in Alaskan reindeer. In 1925, he brought a boatload of wild caribou bulls from the Yukon Valley to Nunivak Island for cross-breeding with reindeer.

While in charge of the Reindeer Experiment Station at the Agricultural College (now the University of Alaska), he conducted nutritional studies with musk oxen and Dall's mountain sheep, as well as with reindeer. He spent two seasons on Kenai Peninsula on moose range examination, and carried on similar work relating to caribou and mountain sheep in central Alaska.

Palmer was author or joint author of publications on range resources and management, the western range as a home for wildlife, and on animal and plant resources of Alaska, particularly the reindeer and their care. A manuscript report on a "Study of the Alaska Tundra with Reference to its Reactions to Reindeer and Other Grazing" awaits publication by the Fish and Wildlife Service.

In World War I, Palmer was in active service with the U. S. Naval Reserve in 1918; he was retained on the inactive list until 1921. In connection with the Alaskan work referred to, he served also as fur warden in enforcing laws and regulations protecting fur-bearing animals in the Territory.

At the time of his death or in comparatively recent years, he was a member of the following organizations: American Association for the Advancement of Science, American Forestry Association, American

Geographical Society, Ecological Society of America, Society of American Foresters, Society of Mammalogists and the Wildlife Society.

He is survived by Inez Muriel Hodges Palmer, to whom he was married at Fairbanks, Alaska, in 1934; there are no children.

W. L. McATEE
FRANK DUFRESNE

SCIENTIFIC EVENTS

THE PROTECTION OF WILDLIFE IN GREAT BRITAIN

A MEMORANDUM drawn up by the British Ecological Society on wildlife conservation and ecological research from the national standpoint, as reported in *The Times*, London, states that the protection, scientific study and intelligent use and enjoyment of native plant life and animal life can only be brought about satisfactorily if the State takes a leading responsibility. It is pointed out that local or private bodies, however well informed, are not in a position to discover, or to hold, the correct balance between the complex and conflicting interests which are deeply involved in many wildlife problems. The memorandum reads:

There appears to be no other satisfactory method than to place the responsibility for advice and coordination upon a separate body acting under the Privy Council. It is recommended that a limited number of areas should be selected which are of sufficient scientific importance to warrant their acquisition by the State for the primary purpose of the conservation and scientific study of the principal types of plant and animal community represented in this country. These national reserves should be managed by a national service of conservators and wardens, under the direction of a national authority, who should proceed under powers similar to those employed for the acquisition of land for State forests. A national biological survey should be established to concern itself with the constantly changing wild and naturalized flora and fauna. This body should be charged with fact-finding, research and advice on the conservation, regulation, control and management of plant and animal life in Great Britain.

At least one general ecological research institute with suitable laboratories should be established by and under the powers granted to the proposed national authority. At this institute facilities should be provided for investigations by workers from the universities and the closest touch should be maintained between the institute and the university departments carrying on ecological research, including the development of humane methods of pest control. There should be established, under a Committee of the Privy Council, an Ecological Research Council as the national authority to cover the vast and hitherto neglected field of research. The pressing need is to extend the field of biological research beyond that now covered. With good sense and sound management overlapping of work or competition for money should never arise.

COMMISSIONS IN THE MEDICAL DEPARTMENT, REGULAR ARMY

1. The Surgeon General invites attention of all Medical Department officers and former officers, other than those retired, of both male and female component corps to War Department Circular 243, dated 10 August 1945. Subject: "Interests in Commissions in the Regular Army," a summary of which follows:

(a) Present indications are that a number of outstanding officers who have proved their capabilities in this emergency will be needed in the Regular Army peacetime establishment. Until appropriate legislation is enacted, the War Department can not announce the conditions which will govern selection of these officers or the number required. However, it is desired that officers who have served in the emergency, whether or not they are still on active duty, be given the opportunity of indicating their interest in obtaining a Regular Army commission. An officer making such a statement of interest may go off active duty or remain in the service without prejudice to his chances of being tendered a commission when legislation is enacted. It is the intention of the War Department that the fact that an officer has not remained in active service will not affect the grade to be offered or the position he will occupy on the promotion list.

(b) The plan for selecting and integrating officers into the Regular Army officers corps, as well as the size and composition of that corps, will finally be determined by Congress. The War Department will recommend that these officers integrated into the Regular Army be of such age and physical condition as will permit them to serve for a reasonably long period before being retired. No officer will be appointed in a grade higher than that which he held in wartime.

(c) The content of this circular will be brought to the attention of every officer at the earliest opportunity.

2. Officers currently on active military duty and who are interested in being considered for commission in the Regular Army, following enactment of appropriate legislation, may submit a statement of interest to their immediate commanding officer as outlined in the above mentioned circular.

3. Officers and former officers other than those retired who have served since 7 December 1941, and who have been relieved from active military duty under honorable conditions, may submit their statement of interest as outlined in the above mentioned circular direct to The Adjutant General, Washington 25, D. C.

4. The submission of a statement of interest in a Regular Army commission in no way obligates an officer to apply for such a commission at any time.

5. At such time when the policies establishing the conditions and procedures for selection and integration of officers into the Regular Army, Medical Department, are finalized, the Surgeon General will make immediate announcement in this publication.

THE COOPERATIVE COMMITTEE ON SCIENCE TEACHING OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE Cooperative Committee on Science Teaching consists of representatives from different organizations of scientists. These representatives are recommended to the American Association for the Advancement of Science and appointed by the Executive Committee. The following are members of this committee. Others will probably be added as recommended by their organizations. It is understood that the committee will meet in October, 1945, to organize itself and to make plans.

Professor K. F. Lark-Horovitz, head of the department of physics, Purdue University, Lafayette, Indiana. (American Association of Physics Teachers.)

Glen Warner, Woodrow Wilson Jr. College, Chicago. (American Association of Physics Teachers.)

Professor Lloyd W. Taylor, head of the department of physics, Oberlin College, Ohio. (American Institute of Physics.)

Professor Raleigh W. Schorling, University of Michigan. (Mathematical Association of America.)

Professor E. H. C. Hildebrandt, department of mathematics, Northwestern University, Evanston, Ill. (National Council of Teachers of Mathematics.)

Professor B. S. Hopkins, department of chemistry, University of Illinois. (American Chemical Society.)

Professor L. L. Quill, head of the school of chemistry, Michigan State College, Lansing. (Division of Chemical Education, American Chemical Society.)

Professor Glenn W. Blaydes, department of botany, The Ohio State University. (Botanical Society of America.)

Professor George A. Thiel, head of the department of geology, University of Minnesota. (Geological Society of America.)

Dr. E. C. Stakman, University of Minnesota. (Executive Committee of the A.A.A.S.)

Dr. R. J. Havighurst, division of human relations, University of Chicago. *Chairman.*

PLANS FOR THE FUTURE OF THE NEW YORK BOTANICAL GARDEN

POSTWAR plans for the New York Botanical Garden which involve a minimum of $6,580,000 in capital expenditure and new endowment are described in the *Garden Week Report*. Of this sum, $1,680,000 is included in the post-war capital budget of the City of New York. The balance of $4,900,000, which includes $300,000 to enable the Garden to participate in the city's expenditure, will be sought through private subscription. The money thus raised will be designated as the Fiftieth Anniversary Fund. The Honorable John W. Davis, former Ambassador to Great Britain, has accepted the chairmanship of a national committee of sponsors for the raising of this sum.

A new museum building to cost $977,500 is planned, and in addition the relocation of roads and construction of new bridges, a new rose garden on the west side of the grounds adjacent to the other plantings, and a new exhibition greenhouse to enable the garden to present more effective displays and to accommodate the Sunday crowds.

A restaurant and a public rest-room also are among the plans. Numerous other additions and improvements include enlarging the size and scope of the monthly *Journal*.

This program of development involves the capital expenditure of $2,305,000 for improvements to physical plant, grounds and equipment.

The balance of $4,275,000 in new permanent funds is desired for the following projects:

To expand the garden's laboratories for research in plant diseases, plant breeding and plant physiology.

To establish seven new curatorships and two assistant posts on the scientific staff.

To create a scholarship fund to foster the advanced training of potential leaders in the plant sciences.

To develop, through more effective display, greater interpretative use of the museum, which is the only public museum in this country exclusively devoted to botany.

To enhance the series of special outdoor gardens and displays of such plants as azaleas, rhododendrons, irises, dogwoods, peonies, roses, dahlias, hardy asters and chrysanthemums, of which the garden already has exceptional collections, and of others which might be established.

The curatorships contemplated include chairs in South American tropical botany, African botany, plants of Eastern Asia, economic botany, fossil botany, in which the garden is recognized as having one of the world's finest collections of specimens, and cryptogamic botany. Other positions called for include a curator of education to plan, coordinate and expand the program of formal and informal public education and information services, and an assistant custodian of the herbarium of more than two million specimens.

Although the annual maintenance costs of the garden are largely met by city appropriations, the educational and scientific work is chiefly dependent on private support. Since 1930 its annual income has shrunk about $75,000 a year, necessitating sacrifices of essential personnel and other economies

which can not be continued without deterioration of invaluable botanical materials and permanent impairment of its basic work.

To meet this situation, and at the same time enable the institution to fulfill its obvious responsibilities to science, education and the public, the Garden's permanent endowment funds must be increased from $4,275,000 to at least $7,000,000, and urgent physical improvements made to the extent of $2,305,000 in its plant, grounds and equipment.

SCIENTIFIC NOTES AND NEWS

THE Theobald Smith Gold Medal of the American Academy of Tropical Medicine has been awarded to Dr. Charles M. Wenyon, protozoologist and retired director of the Wellcome Foundation Research Laboratories of London, England. In view of the circumstance that the state of Dr. Wenyon's health makes a journey to the United States to receive the presentation in person impossible, arrangements will be effected for a presentation in London through the United States Embassy.

DR. CHARLES M. POMERAT, professor of anatomy at the School of Medicine at Galveston of the University of Texas, has been elected a corresponding member of the Mexican Academy of Science. Dr. Pomerat recently spent several weeks in Mexico City in the study of tropical diseases and in assisting in establishing laboratories for tissue culture experimentation.

AT the recent meeting of the Society for the Study of Development and Growth, the following officers were elected for the year 1945–1946: *President,* Dr. Albert F. Blakeslee, Smith College; *Secretary,* Dr. J. Walter Wilson, Brown University; *Treasurer,* Francis O. Schmitt, Massachusetts Institute of Technology.

THE statement that Dr. George B. Pegram would become acting president of Columbia University was reported erroneously in the press and was announced in the issue of SCIENCE for August 31. This statement was based on the fact that it was planned in case of emergency incapacitating the president, in succession, the dean of the Graduate Faculties, the dean of Columbia College, etc., should take on the duties of the president. Since a regular meeting of the trustees of the university will occur on October 1, when President Butler's retirement goes into effect, the trustees will at that time and not before determine who shall become president in the interim before a new president can be obtained.

DR. P. DUNSHEATH, director and chief engineer of W. T. Henley's Telegraph Works Co., has been appointed president of the British Institution of Electrical Engineers.

DR. OSCAR RIDDLE has retired from the Department of Genetics of the Carnegie Institution of Washington. Starting in September, under the auspices of the Division of Cultural Relations of the Department of State, he will become visiting professor from the United States in Brazil, Uruguay and Argentina.

DR. W. C. PRICE, formerly associate of the Rockefeller Institute for Medical Research, has been appointed associate research professor of biology at the University of Pittsburgh. He will continue his work on plant viruses as a part of the natural sciences research program of the university.

DR. FREDERICK E. EMERY, associate professor of physiology at the University of Buffalo School of Medicine, has been appointed professor of physiology and head of the department of physiology and pharmacology of the School of Medicine of the University of Arkansas, Little Rock.

DR. REYNOLD A. JENSEN, associate professor of child psychiatry in the department of pediatrics of the University of Minnesota, under the auspices of a grant from the Rockefeller Foundation, is visiting lecturer in child psychiatry during August and September at the School of Medicine of the University of Utah.

DR. LAURENCE MCKINLEY GOULD, for the past thirteen years professor of geology and geography at Carleton College, has been elected president of the college. Dr. Duncan Stewart, associate professor of geology at Lehigh University, who has twice previously been a member of the faculty of Carleton College, has succeeded him as professor of geology and chairman of the department.

DR. GEORGE C. KENT, of the Iowa State College, has been appointed professor of plant pathology at Cornell University.

DR. O. W. BRANDHORST has been appointed to succeed Dr. Benno E. Lischer, retired, as dean of the School of Dentistry of Washington University.

THE department of mining and civil engineering of the Michigan College of Mining and Technology at Houghton has been divided, and a department of engineering administration has been established which will include work previously assigned to the departments of economics and government and of psychology and sociology. Professor Murray Riddell will be the head of the department of mining; Professor W. C. Polkinghorne head of the department of civil engi-

neering, and Associate Professor E. J. Townsend head of the department of engineering administration.

GEORGE WESLEY AUSTIN, of Birmingham, has been elected Goldsmiths professor of metallurgy at the University of Cambridge to succeed Professor R. S. Hutton, who recently retired.

THE retirement is announced of Professor L. Bairstow, Zaharoff professor of aeronautics in the University of London.

PROFESSOR ERNEST HORACE LAMB, for thirty-two years professor of civil and mechanical engineering at Queen Mary College, London, will retire at the end of the present session. As already announced, he will be succeeded by Dr. Edmund Giffen, since 1940 director of research at the Institution of Automobile Engineers' Laboratories at Brentford.

DR. JOHN A. SHELLENBERGER, professor of milling industry, has been appointed head of the department at the Kansas State College, Manhattan, to succeed Dr. E. G. Bayfield, who has resigned.

AT Rutgers University associate professors have been appointed to full professorships as follows: Dr. James Boyd Allison, professor of physiology and biochemistry and director of the Rutgers Bureau of Biological Research; Dr. Gilbert Harold Ahlgren, professor of farm crops and research specialist in farm crops; Dr. Helgi Johnson, professor of geology and director of the Geological Museum, and Dr. William Riemann, III, professor of analytical chemistry. Dr. Ellwood Meachem Hammaker, analytical chemist for the General Electric Company, has been appointed assistant professor of chemistry.

DR. HUGH R. LEAVELL, Louisville, Ky., director of the Jefferson County Board of Health, who has been on leave with the UNRRA in Europe, has been appointed an assistant director for the medical sciences of the Rockefeller Foundation.

DR. W. F. B. MCLINTOCK, since 1937 deputy director of the Geological Survey of Great Britain and of the Museum of Practical Geology, has been appointed director.

THE committee on professional education of the American Public Health Association announces that Professor Charles-Edward Amory Winslow, chairman of the department of public health of Yale University, for thirty years Anna M. R. Lauder professor of public health, has been appointed counsellor in charge of a group of investigators who will compile data to be used in creating a body to accredit institutions to give degrees of master of public health, doctor of public health and the diploma in public health.

DR. J. H. SIMONS, professor of physical chemistry at the Pennsylvania State College, has been named director of the Fluorine Research Laboratories. Under the direction of Dr. Simons these laboratories have been engaged for some time on fundamental research and development in fluorine chemistry. Fellowships for research are provided and research projects undertaken.

DR. WILLIAM RANDOLPH TAYLOR, of the University of Michigan, has received a card dated August 6 from Professor H. H. Gran, the distinguished Norwegian marine biologist, indicating that in spite of wartime difficulties and his advanced age of seventy-five years he is well and happy.

DR. JOSEPH STOKES, JR., professor of pediatrics in the Medical School of the University of Pennsylvania, gave the first lectures of the Intermountain Pediatric Lectureship of the Medical School of the University of Utah on July 16 and 17 on "Studies of Infectious Hepatitis" and "The Use of Gamma Globulin in Infectious Hepatitis and Other Communicable Diseases." Dr. Ashley Weech, professor of pediatrics and head of the Children's Research Foundation of the University of Cincinnati, presented two lectures on July 26 and 27 on "The Physiologic Consequences of Inadequate Dietary Protein" and "The Role of Cortical Development in the Behavior of the Infant."

THE fifty-first summer meeting of the American Mathematical Society will be held at the New Jersey College for Women, Rutgers University, New Brunswick, N. J. The summer meeting of the Institute of Mathematical Statistics will also be held at the same place on September 16. Sessions will begin on Saturday, September 15, at 9:30 A.M. and continue through Monday morning. In addition to the addresses previously announced for Saturday, by Professor S. S. Chern, Professor Samuel Eilenberg and Professor Witold Hurewicz, there will be a symposium on "Recent Developments in Numerical Methods" at 2:00 P.M. on Sunday, consisting of three addresses: "Interpolation, Smoothing and Curve Fitting," by Professor I. J. Schoenberg, of the University of Pennsylvania; "Laurent Expansions of Algebraic Functions," by Professor Hans Rademacher, of the University of Pennsylvania, and "Numerical Solutions of Integral Equations," by Professor A. T. Lonseth, of Northwestern University.

IT is reported in *Nature* that an Anglo-French conference on cosmic rays will be held in the H. H. Wills Physical Laboratory, University of Bristol, on September 25, 26 and 27. It is hoped that some ten French delegates will attend, including Professor P. Auger, Professor F. Joliot and Professor I. Curie-Joliot.

THE Special Libraries Association published in August "A List of Subject Headings for Chemistry Libraries." It was compiled by a committee of the Section of Chemistry of the Science-Technology Group of the Special Libraries Association, under the chairmanship of Mrs. Grace R. Cameron, of the Louisiana State University Library. This list was compiled for use in assigning subject headings to the entries in a catalogue of books, pamphlets and other literature in a chemical library. General or main headings are used which can be expanded as needed. Subdivisions which may be used under general headings are also given. Examples of expansions for specialized fields such as dyes, paper and rubber are included. This publication is for all college, university, public and special libraries containing any chemical material.

THE Georgia Power Company has made a gift of $100 to the Alumni Foundation of the Georgia Institute of Technology at Atlanta. The fund will be used largely to buy equipment to further electrical research at the school.

SPECIAL ARTICLES

ORAL ADMINISTRATION OF PENICILLIN[1]

ALTHOUGH it was originally assumed that penicillin could not be administered orally because of its rapid destruction by gastric acid,[2] a number of investigators have reported effective blood levels when relatively large doses of penicillin by mouth were given by various methods (Libby[3]; Charney *et al.*[4]; McDermott *et al.*[5]; György *et al.*[6]; Little *et al.*[7]; Burke *et al.*[8] and Moses[9]). In a recent review of some of these investigators[10] it was stated that although oral penicillin was therapeutically effective when given either as a suspension in a digestible oil or when accompanied by one of the mild antacids, the most favorable vehicle had not yet been determined. McDermott and his collaborators[5] found no significant difference between the administration of penicillin by the oral route when it was given (*a*) in corn oil; (*b*) in water; (*c*) in water preceded by a buffer; and (*d*) in peanut oil and 4 per cent. beeswax. The authors, however, stated that the height of the penicillin concentrations in the blood two hours after ingestion of the oil and oil in beeswax preparations suggested that the duration of penicillin activity may be prolonged by the use of these vehicles by mouth in a manner similar to the prolongation which, as Romansky[11] showed, follows the intramuscular injection of penicillin in oil and beeswax. Selection of the best oral method from those previously reported is difficult because of the lack of an adequate number of blood level determinations in the same subjects with the various procedures.

In this communication the results of administration of penicillin mixed with aluminum hydroxide are compared with the results of administration of penicillin in water. When aluminum hydroxide was given one-half hour before ingestion of penicillin and not mixed with it, no significant advantage was detected by blood level curves. A few tests of penicillin by mouth with other procedures have been included in the graphs. The importance of using the same subject with different methods is revealed by the large individual variation with the same dose of penicillin. Thus, a man weighing 200 pounds would be expected to have a lower blood level than one weighing 100 pounds, irrespective of age. The factor of relationship to eating was kept relatively constant in this study. Most of the observations were made one to two hours after breakfast or lunch.

METHODS

The penicillin was dissolved in tap water, either (1) by inserting 4 cc of water into the 100,000 unit ampoule by a hypodermic syringe, withdrawing the contents and rinsing the remaining penicillin solution in the ampoule with an additional 4 cc of water, or (2) by removing the metal band and rubber cork from the bottle and dissolving the 100,000 units of penicillin in a teaspoonful of water and then rinsing

[1] This investigation was aided by grants from the Josiah Macy Jr. Foundation and the Foundation for the Investigation of Chronic Pulmonary Diseases. The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutic and Other Agents of the National Research Council. The aluminum hydroxide used in this investigation was largely supplied to us by Wyeth, Inc.

[2] E. P. Abraham, E. Chain, C. M. Fletcher, A. D. Gardner, N. G. Heatley, M. A. Jennings and H. W. Florey, *Lancet*, 2: 177, August 16, 1941.

[3] R. L. Libby, SCIENCE, 101: 178, February 16, 1945.

[4] J. Charney, H. E. Alburn and F. W. Bernhart, SCIENCE, 101: 251, March 9, 1945.

[5] W. McDermott, P. A. Bunn, M. Benoit, R. DuBois and W. Haynes, SCIENCE, 101: 228, March 2, 1945.

[6] P. György, H. N. Vandergrift, W. Elias, L. G. Colio, F. M. Barry and J. D. Pilcher, *Jour. Am. Med. Asn.*, 127: 639, March 17, 1945.

[7] C. J. H. Little and G. Lumb, *Lancet*, 1: 203, February 17, 1945.

[8] F. G. Burke, S. Ross and C. Strauss, *Jour. Am. Med. Asn.*, 128: 83, May 12, 1945.

[9] C. Moses, *Jour. Am. Med. Asn.*, 128: 52, May 5, 1945.

[10] Editorial, *Jour. Am. Med. Asn.*, 127: 1129, April 28, 1945.

[11] M. F. Romansky and F. E. Rittman, SCIENCE, 100: 196, 1944.

the bottle with an additional one or two teaspoonfuls of water. The final 8 cc, or two to three teaspoonfuls of penicillin solution, were then mixed in a glass with one tablespoonful of aluminum hydroxide.[12] After thorough mixing with a spoon or fork, a quarter of a glass of water is added and the solution drunk in this form. When 50,000 units were administered the total amount from the ampoule was divided in two equal parts and one half the quantity ingested. When blood level determinations were made the first 2 cc of the 4 cc of solution instilled into the bottle were withdrawn accurately with a tuberculin or a two cc syringe. The serial broth dilution method of blood level analysis described by Hobby[13] was used.

RESULTS

The subjects consisted in the main of patients with bronchial asthma, bronchiectasis and pulmonary fibrosis, who were being treated with penicillin aerosol and oral penicillin. The total number of blood levels was 314, of which 250 were from patients and 64 from normal individuals. In Chart 1 the blood levels after administration of 50,000 units of penicillin mixed with aluminum hydroxide were compared to the results on the same subjects when penicillin was taken dissolved in water alone. As will be seen from the chart, a significantly higher blood level was present from ½ to 2 hours after ingestion of the drug mixed with aluminum hydroxide. The results of ingestion of 50,000 units of penicillin mixed with aluminum hydroxide in a miscellaneous group in which both the same and different subjects were used is revealed in Chart 2. It will be seen that the penicillin blood level curve with aluminum hydroxide was again higher, although this chart included patients who were not treated by all the various methods.

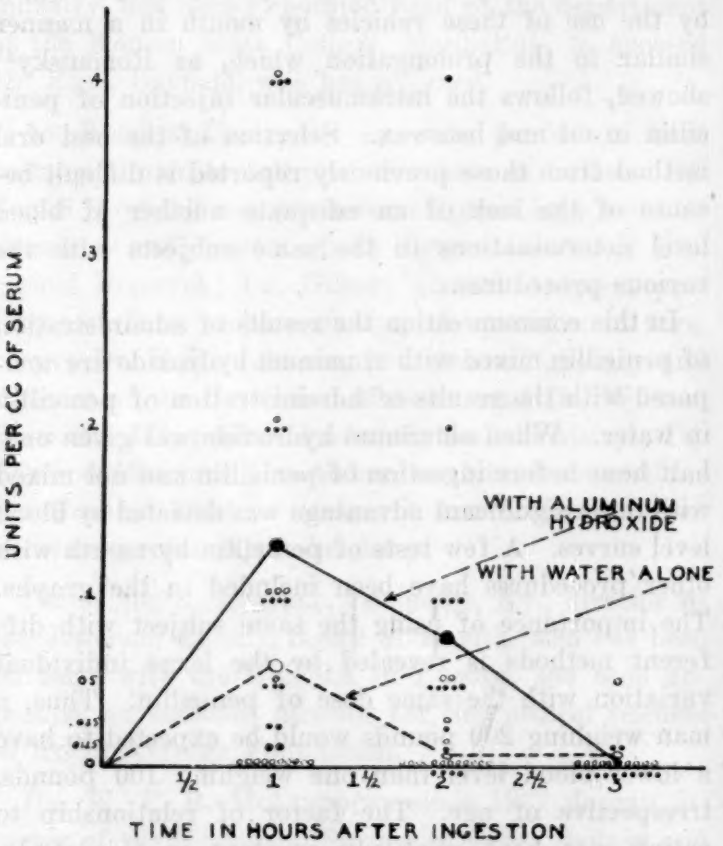

CHART 1. Comparison of penicillin blood levels on the same 14 patients after oral administration of 50,000 units of penicillin with (A) aluminum hydroxide and (B) water alone. The curves represent a total of 88 blood level determinations.

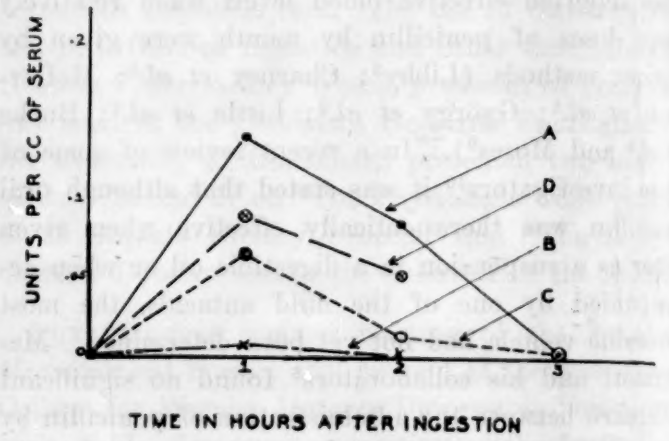

CHART 2. Comparison of penicillin blood levels on miscellaneous groups of patients after oral administration of 50,000 units of penicillin. (A) Mixed with aluminum hydroxide, 16 cases. (B) Aluminum hydroxide given previously, not mixed, 5 cases. (C) With water alone, 18 cases. (D) With $NaHCO_3$, egg and milk, 7 cases. The curves represent a total of 148 blood level determinations taken during 55 tests.

The results of ingestion of 100,000 units of penicillin mixed with aluminum hydroxide with comparative data on the same patients after 100,000 units were administered in water are illustrated in Chart 3. The blood level of penicillin when 100,000 units were given mixed with aluminum hydroxide was higher on the average than when given with water, but when different subjects were at times used for different tests, as shown in Chart 4, the penicillin blood level curves do not reveal the superiority of the aluminum hydroxide mixing method. This chart is evidence of the failure of the method of using different people for different tests, since when the same people are used for comparison, as shown in Charts 1 and 3, the aluminum hydroxide method showed a higher blood level. A more clear-cut difference was found when the smaller dose, 50,000 units, was given.

[12] A mixture of aluminum hydroxide and kaolin has been found to be better tolerated and at least as effective an adsorbent of penicillin as pure aluminum hydroxide. One tablespoonful of Kaomagma is mixed with 100,000 units of penicillin and stirred for a full minute or more. The quantity of water added has been increased to three-quarters of a glass in order to avoid local irritating effects, such as red tongue and pharynx, which are at times apparently produced by contact of the mucous membrane with concentrated solutions. A quarter to half a glass of water is also ingested afterwards.

[13] H. J. Greene and G. L. Hobby, *Proc. Soc. Exp. Biol. and Med.*, 57: 282, 1944.

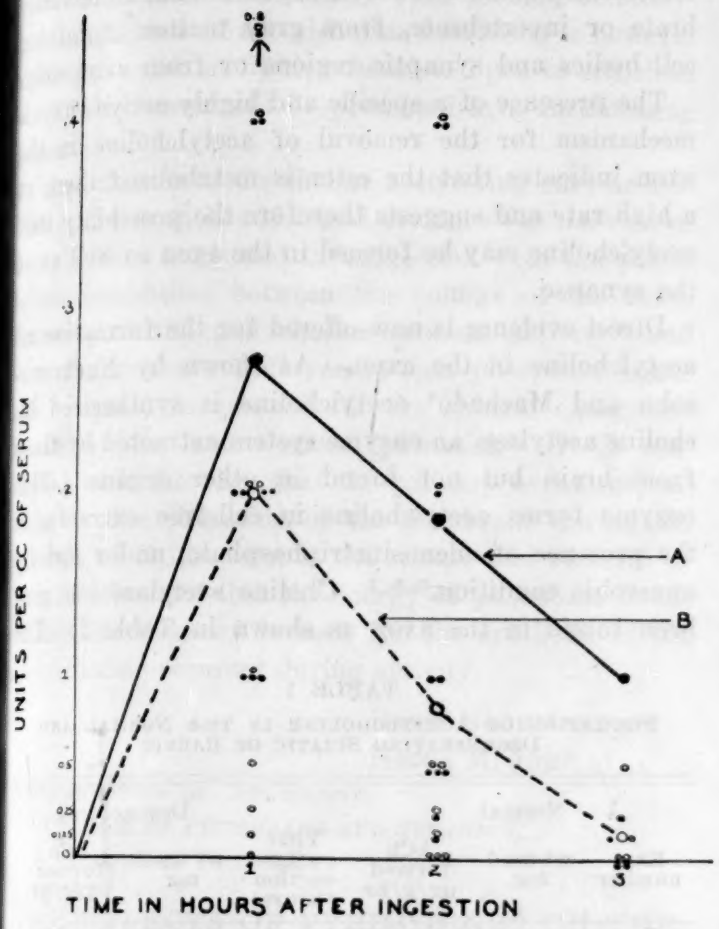

CHART 3. Comparison of penicillin blood levels on the same 9 patients after oral administration of 100,000 units of penicillin with (A) aluminum hydroxide; (B) water alone. The curves represent a total of 47 blood levels.

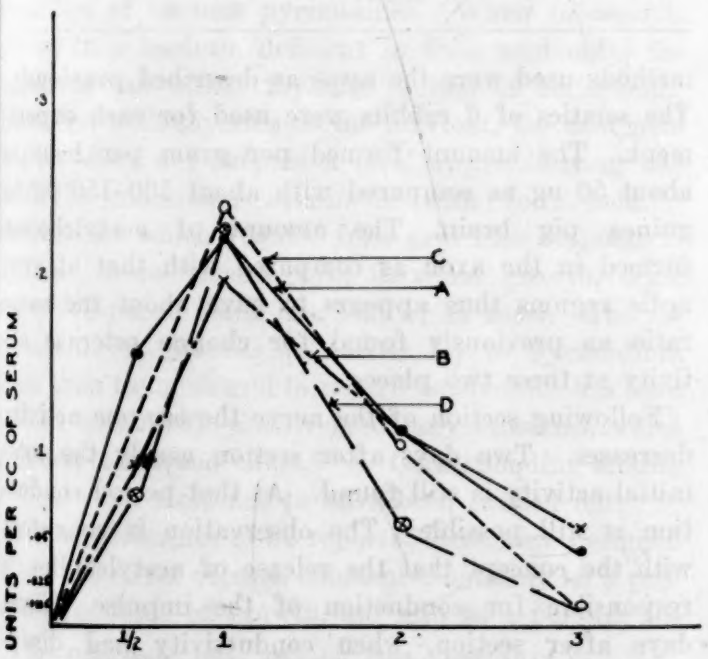

CHART 4. Comparison of penicillin blood levels on miscellaneous groups of patients after oral administration of 100,000 units of penicillin. (A) Mixed with aluminum hydroxide, 21 cases. (B) Aluminum hydroxide given previously, not mixed, 13 cases. (C) With water alone, 14 cases. (D) With $NaHCO_3$, egg and milk, 4 cases. The curves represent a total of 166 blood level determinations taken during 58 tests.

When the data were examined from the point of view of whether or not an effective blood level was found by the various methods, it was seen that in 43 of 44 cases in which aluminum hydroxide was mixed with penicillin a measurable blood level was obtained, whereas in 19 out of 58 cases in which the penicillin was dissolved in water and taken either with or without previous ingestion of aluminum hydroxide or sodium citrate, no penicillin was found in the blood.

The value of mixing penicillin with aluminum hydroxide is, therefore, indicated both by the frequency of effective blood levels and by the consistency with which a measurable blood level was obtained even with a dose as moderate as 50,000 units, which is less than that frequently used in other methods of oral administration in adults.

Although it has long been known that penicillin is destroyed in the large intestine, a recent report of Loewe[14] disclosed that large doses of penicillin administered in a suppository were followed by demonstrable blood levels. This stimulated us to try a series of 5 cases, dissolving 50,000 units of penicillin in 20 cc of water and introducing it by catheter and syringe into the rectum. No demonstrable blood level was found at the end of one, two or three hours in the five individuals tested in this manner. From these experiments it was evident that the administration of penicillin in aqueous solution by rectum was an inefficient and impracticable method.

DISCUSSION

Complete neutralization of gastric acid to prevent the destructive effect of hydrochloric acid on penicillin would require relatively large doses of alkaline medication. When penicillin is mixed with aluminum hydroxide a protective effect is apparently exerted by this colloidal substance due to adsorption of penicillin on aluminum hydroxide and due to its antacid effect on that portion of gastric acid with which the penicillin-aluminum hydroxide mixture comes in contact. No significant advantage was detected when aluminum hydroxide was used as an antacid prior to administration of penicillin, a finding which is consistent with the results of McDermott *et al.*[5]

In the clinical use of this procedure, nausea and indigestion have been encountered at times when one tablespoonful of aluminum hydroxide was administered at three-hour intervals, either with 50,000 or 100,000 units of penicillin. In these cases the dosage was lowered to two teaspoonfuls, which is generally well tolerated, either at three or, if desired, at two-hour intervals.[12] Further investigations in progress aim at the production of still higher blood levels than

[14] L. Loewe, E. Alture-Werber and P. Rosenblatt, *Jour. Am. Med. Asn.*, 128: 18, May 5, 1945.

those here reported. Had it been practical to give penicillin before breakfast and take the necessary blood levels for two- and three-hour periods under fasting conditions, better results would presumably have been obtained. However, since the clinical use of oral penicillin requires administration one or two hours after eating as well as before meals, these findings are applicable to the actual conditions of treatment. To provide optimal conditions for the absorption of penicillin, by mouth, the patient should be instructed to avoid fat in the diet in order not to delay the emptying time of the stomach, and also to take the penicillin one hour before eating and two hours after eating.

SUMMARY

A convenient, practical and effective procedure of administering penicillin by mouth consists of mixing the drug with one tablespoonful of aluminum hydroxide. Substantially higher blood levels are obtained following a 50,000 and a 100,000 unit dose of penicillin with this method than after administration of the drug dissolved in water, either with or without previous ingestion of a mild antacid, such as aluminum hydroxide. Adsorption of penicillin on aluminum hydroxide appears to exert a local protective effect against that portion of gastric acid with which it comes into contact.

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ON THE FORMATION OF ACETYLCHOLINE IN THE NERVE AXON

THE high concentration of choline esterase in the axon and its exclusive localization at the neuronal surface is one of the essential facts in favor of the concept that the release and the removal of acetylcholine is an intracellular process generating flow of current, the action potential.[1] Nachmansohn and Rothenberg[2, 3] have recently shown that the esterase of the nerve axon is specific for acetylcholine: if the enzyme activity is tested on a number of esters, a typical pattern is obtained distinctly different from that of other unspecified esterases. This specific choline esterase is found, either exclusively or predominantly, in all nerve tissue whether taken from mammalian brain or electric organ of fish, from vertebrate or invertebrate, from gray matter containing cell bodies and synaptic regions or from axon only.

The presence of a specific and highly active enzyme mechanism for the removal of acetylcholine in the axon indicates that the ester is metabolized there at a high rate and suggests therefore the possibility that acetylcholine may be formed in the axon as well as at the synapse.

Direct evidence is now offered for the formation of acetylcholine in the axon. As shown by Nachmansohn and Machado[4] acetylcholine is synthesized by choline acetylase, an enzyme system extracted by them from brain but not found in other organs. This enzyme forms acetylcholine in cell-free extracts, in the presence of adenosinetriphosphate, under strictly anaerobic condition.[5, 6, 7] Choline acetylase has now been found in the axon as shown in Table 1. The

TABLE 1

FORMATION OF ACETYLCHOLINE IN THE NORMAL AND DEGENERATING SCIATIC OF RABBIT

	Normal			Degenerated	
Exp. number	wt used mg	ACh formed μg/g/hr	Time after section (hours)	wt used mg	ACh formed μg/g/hr
1	395	60.0	0	392	61.0
	322	59.0	(control)	328	50.0
2	380	19.0	64	620	4.9
3	558	20.0	72	564	2.6

methods used were the same as described previously. The sciatics of 6 rabbits were used for each experiment. The amount formed per gram per hour is about 50 μg as compared with about 100–150 μg in guinea pig brain. The amount of acetylcholine formed in the axon as compared with that at synaptic regions thus appears to have about the same ratio as previously found for choline esterase activity at these two places.

Following section of the nerve the enzyme activity decreases. Two days after section nearly the total initial activity is still found. At that period conduction is still possible. The observation is consistent with the concept that the release of acetylcholine is responsible for conduction of the impulse. Three days after section, when conductivity had disappeared, the enzyme activity had lost only a part of the initial value. The results and conclusions are in

[1] D. Nachmansohn in R. S. Harris and K. V. Thimann, *Vitamins and Hormones*, New York, 3, 1945. In press.
[2] D. Nachmansohn and M. A. Rothenberg, SCIENCE, 100: 454, 1944.
[3] *Idem, Jour. Biol. Chem.*, 158: 653, 1945.
[4] D. Nachmansohn and A. L. Machado, *Jour. Neurophysiol.*, 6: 397, 1943.
[5] D. Nachmansohn, H. M. John and H. Waelsch, *Jour. Biol. Chem.*, 150: 485, 1943.
[6] D. Nachmansohn and H. M. John, *Proc. Soc. Exp. Biol. and Med.*, 57: 361, 1944.
[7] *Idem, Jour. Biol. Chem.*, 158: 157, 1945.

contrast to those of Feldberg[8]; his method of studying the problem of acetylcholine formation is however inadequate and his figures therefore open to criticism. A full discussion will be presented in a forthcoming paper.

The presence of the choline acetylating enzyme system in the axon is additional evidence for the role of acetylcholine suggested in connection with the parallelism established between the voltage of the nerve action potential and choline esterase activity[9a] and with the evidence that energy-rich phosphate bonds are adequate to account for the electric energy released by the nerve action potential.[9b] It is consistent with the view that the primary event responsible for the alteration of the membrane during the passage of the impulse is the release and removal of acetylcholine and that the energy of phosphate bonds during the recovery is used for the synthesis of the acetylcholine removed during activity.

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THE EFFECTS OF PYRIMIDINES ON THE GROWTH OF LACTOBACILLUS CASEI

INVESTIGATIONS in these laboratories concerning the specificity of the response of *Lactobacillus casei* to folic acid have led to a study of the effects on this organism of various pyrimidines. When *L. casei* is grown in a medium deficient in folic acid only, the organism can utilize thymine in lieu of folic acid.[1] However, with thymine as the nutrient, the acid production does not surpass a level approximating one half the maximum attainable with folic acid.[1, 2] Enterococci which require folic acid also respond to thymine, some strains with maximal growth, some with a response much like that of *L. casei*. The response of *S. faecalis* (*S. lactis R*) to pyrimidines other than thymine and to related compounds has been studied without the discovery of any substance which produces a marked effect.[1,3,4] Corresponding studies with *L. casei* seem not to have been carried out.

The experiments to be reported here were designed to test the effect of each substance, not only as a possible stimulator of growth, but also as a possible inhibitor of the growth elicited with thymine or folic acid as nutrilite. A medium of approximately the same composition as that of Landy and Dicken[5] was used. Each substance, in amounts ranging from 0.0005 to 1 mg, was added to 10 ml of (1) the basal medium, (2) medium containing thymine in an amount sufficient to produce the full response (10 γ) and (3) medium containing folic acid sufficient to give about half-maximal growth (0.001375 microgram unit).[6]

Among the more than one hundred substances tested, twenty or more were found to give a significant biological response of one kind or another. Some examples of the experimental results are given in Table 1.

TABLE 1

RESPONSE OF *L. casei* TO VARIOUS PYRIMIDINES

Substance	Concentration mg/ 10 ml	Effect of pyrimidine in various media Change of titre per cent. Unsupplemented	With thymine*	With folic acid†
Thymine	0.01	+500	0	+20
5-Methyl cytosine	0.1	+200	..	..
5-Methyl isocytosine	0.2	+300	0	+10
5-Methyl-2,4-diamino-pyrimidine	1.0	+300	−20	+20
5-Methyl-2-thio-4-oxy-pyrimidine	0.05	− 30	+10	+10
5-Methyl-2,4-dithio-pyrimidine	0.25	+ 20	−25	0
5-Methyl-2-oxy-4-thio-pyrimidine	0.004	+300	+15	0
5-Methyl-2,4-dioxy-6-imino-pyrimidine	1.0	− 10	0	0
5,6-Dimethyl 2,4-dioxy-pyrimidine	1.0	0	0	0
2,5-Dimethyl-4-oxy-pyrimidine	1.0	+ 30	+10	+10
5-Hydroxy uracil	1.0	− 50	−70	−75
5-Amino uracil	1.0	− 50	−25	−55
5-Carbamido uracil	1.0	− 50	−55	0
5-Chloro uracil	1.0	+ 45	−93	+20
5-Bromo uracil	0.2	+ 20	−40	+15
5-Iodo uracil	1.0	0	−40	−20
5-Nitro uracil	0.2	0	−14	−65

* 10 micrograms per 10 ml.
† 0.001375 microgram equivalent per 10 ml.

In the series of compounds which may be regarded as derivatives of thymine in which one or both of the oxygens is replaced by an imino or thio group, many of the members simulate the biological action of thymine. The replacement of oxygen by the imino group appears in each instance to weaken the activity so that approximately ten times as much imino as oxy compound is required to produce a response of the same magnitude. Since the two monoimino compounds are equal in activity and the response of *L. casei* to mixtures of these compounds can be predicted as an additive function of the responses to the individual components, and since 5-methyl-isocytosine

[8] W. Feldberg, *Jour. Physiol.*, 101: 432, 1943.
[9] D. Nachmansohn, R. T. Cox, C. W. Coates and A. L. Machado, (a) *Jour. Neurophysiol.*, 5: 499, 1942, and (b) 6: 383, 1943.
[1] J. L. Stokes, *Jour. Bact.*, 48: 201, 1944.
[2] K. Krueger and W. H. Peterson, *Jour. Biol. Chem.*, 158: 145, 1945.
[3] H. K. Mitchell and R. J. Williams, *Jour. Am. Chem. Soc.*, 66: 271–274, 1944.
[4] T. D. Luckey, G. M. Briggs, Jr. and C. A. Elvehjem, *Jour. Biol. Chem.*, 152: 157, 1944.
[5] M. Landy and D. M. Dicken, *Jour. Lab. Clin. Med.*, 27: 1086–1092, 1942.
[6] As 7.7 per cent. concentrate obtained through the courtesy of Professor R. J. Williams.

produces consistently a slightly greater acid production than does thymine, it appears that the imino compounds act as such and not, as might have been supposed, primarily by deaminization to thymine. The action of the thio compounds is somewhat more complex. Thus, 2-thio- and 2,4-dithiothymine have only slight activity, whereas 4-thiothymine is approximately as active as thymine, perhaps due to the lability of the 4-thio atom.

The introduction of a substituent into the 6-position of the thymine molecule seems, in general, nearly to abolish the activity. Thus a second methyl group as in 2,4-dioxy-5,6-dimethyl or an amino group in the same position renders the compound essentially inactive.

As shown below, if the methyl group of thymine is replaced by an amino or hydroxy group, compounds with a considerable inhibitory activity are produced. The reverse change, replacement of the oxy group in the 2-position by a methyl group, might have been expected to produce a compound with similar properties. However, the compound formed, 2,5-dimethyl-4-oxypyrimidine, is essentially inactive. This is, perhaps, related to the fact that the oxygen atoms of thymine apparently exist in the doubly bonded lactam form.[7] The entrance of a methyl group in the 2-position, therefore, involves a considerable change in the configuration of the molecule, since it results in the elimination of one imide hydrogen atom.

Among the 5-substituted uracils, compounds which may be regarded as derived by the substitution of other groups for the methyl group of thymine, there were found a number of compounds which inhibit the growth of *L. casei*. Isobarbituric acid (5-hydroxyuracil) and 5-aminouracil have approximately the same molecular weight and would be expected to have a spatial configuration similar to that of thymine. Both strongly inhibit the growth of *L. casei*. Moreover, growth can be restored by increasing the concentration of either thymine or folic acid. It is reasonable to suppose, therefore, that these substances exert their action by the displacement of thymine from active enzyme centers or structural elements and suggest the possibility of a metabolic function of the methyl group which can not be performed by the hydroxy or amino groups. Since the effects of these two inhibitors are exerted with either nutrilite, these observations are not inconsistent with Stokes's view of thymine as a product of an enzyme system which involves folic acid as a prosthetic group or coenzyme.[1] That this hypothesis is not an adequate explanation of the action of thymine, however, is brought out by a consideration of the effects of the 5-halogenopyrimidines and of 5-nitrouracil. For example, bromouracil can inhibit completely the growth of *L. casei* with thymine as the nutrient but may have no effect or produce a slight stimulation when folic acid is used as the nutrient. It follows that the growth of *L. casei* with folic acid as nutrient does not depend on an intermediary synthesis of thymine as such. Moreover, nitrouracil can prevent the growth of *L. casei* with folic acid at concentrations which have little or no effect on the growth with thymine. These observations suggest that the two nutrients act, in some fashion, as alternatives rather than as two components of an anabolic system.

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THE THYMUS AND ACETYLCHOLINE SYNTHESIS

THE possible involvement of the thymus in myasthenia gravis has led to the suggestion by Trethewie and Wright[1] that the thymus may influence the formation of acetylcholine (Ach), and by McEachern[2] that it may produce a curare-like substance which interferes with the action of Ach. Experimental evidence concerning the thymus and Ach synthesis is conflicting. Stoerk and Morpeth[3] incubated minced rat brain in Locke solution, with and without added thymoma tissue from a patient who died from myasthenia gravis, and found no significant difference in the amount of Ach synthesized in a three-hour period. Trethewie and Wright,[1] in two experiments, obtained slightly greater yields of Ach when ground brain was incubated with infant thymus than in controls without thymus. In one experiment, using thymus tissue from a person with myasthenia gravis, they obtained a small decrease in Ach formation.[4]

Experiments testing a possible effect of newborn rat thymus on Ach synthesis by brain slices of adult and newborn rats will be reported briefly.

EXPERIMENTAL

In five experiments the brain of an adult rat was split sagittally and each half sliced thinly. The slices of each half were weighed and placed in Locke solution containing glucose 1:500 and eserine 1:5,000. Ground thymus glands from twelve rats less than 24 hours old were added to one lot of slices and both lots

[7] J. R. Loofbourow, Sr. Miriam Michael Stimson, O.P., and Sr. Mary Jane Hart, O.P., *Jour. Am. Chem. Soc.*, 65: 148, 1943.

[1] E. R. Trethewie and R. D. Wright, *Aust. and New Z. Jour. Surg.*, 13: 244, 1944.

[2] D. McEachern, *Medicine*, 22: 1, 1943.

[3] H. C. Stoerk and E. Morpeth, SCIENCE, 99: 496, 1944.

[4] See also Torda, C., and H. G. Wolff, *Proc. Soc. Exp. Biol. and Med.*, 57: 69, 1944 for the effect of ether extract of the thymus on synthesis of acetylcholine.

were shaken in an atmosphere of 95 per cent. O_2—5 per cent. CO_2 for one and one quarter hours at 37° C. Two experiments were performed on newborn rat brain in a similar manner, except that slices of six brains were divided in two lots, one for the control and the other for incubation with thymus tissue.

After incubation the total Ach was obtained by treatment with HCl and the extracts assayed on the isolated heart of *Venus mercenaria*. In each experiment a careful comparison of the effects of the extracts of brain tissue incubated with and without thymus tissue was made and the actual amounts of Ach in the extracts estimated by comparison with known amounts of Ach.

Results

The results are given in Table 1. The amount of

TABLE 1

EFFECT OF NEWBORN RAT THYMUS ON ACH SYNTHESIS BY RAT BRAIN SLICES

	Incubated without added thymus	Incubated with added thymus
	Total Ach, γ/gm	Total Ach, γ/gm
A. Adult brain slices		
Exp. 1	10	10
2	6–7	6–7
3	20	20
4	4–6	4–6
5	5	5
B. Infant brain slices		
Exp. 1	3	3
2	1	1

total Ach normally present in whole, adult rat brain is of the order of 1 to 1.5 gamma per gram; that in newborn rat brain of the order of 0.5 gamma per gram. It may be noted, therefore, that appreciable amounts of Ach were synthesized in all experiments. In each experiment, however, the amounts of Ach obtained from brain slices incubated with or without added thymus tissue are the same. It may be concluded that under the conditions of these experiments normal infant rat thymus neither accelerates nor retards the synthesis of Ach by brain slices.

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A FIBRINOLYTIC ENZYME IN MENSTRUATION AND LATE PREGNANCY TOXEMIA

THE demonstration[1, 2] that prothrombin and fibrinogen are lacking in menstrual discharge suggests that the blood in it has clotted and the clot dissolved. Evidence for the existence of lytic substances to account for its fluidity has been presented by many but has been inconclusive. Fibrinolytic action in the uterus is nevertheless a rational explanation and a proteolytic enzyme might, in addition, account for the great toxicity of the euglobulin fraction of menstrual discharge, which contains altered protein.[3] Such an enzyme might be a product of endometrial injury due to the withdrawal of hormonal support. Its physiological function might be lysis of damaged tissue, including clotted blood, for the purpose of elimination. The toxic by-product, as has been suggested,[4, 5] might be the final cause of menstruation through vascular injury. Since the hormonal situation in toxemia of late pregnancy is entirely analogous to that at the time of menstruation and the generalized vascular changes similar to the local ones in the menstruating endometrium, we have theorized that this disease might be due to a similar toxin.[5] We have been unable to find such a toxin in the circulating blood at the time of menstruation or toxemia. If a proteolytic enzyme, however, were associated with these states it might be demonstrable, since tests for it are so much more sensitive than our criterion for toxicity, which depends upon obtaining an amount lethal to an immature rat.

A simple method was employed in testing for fibrinolytic activity.[6] Fresh plasma from oxalated human venous blood has been our source of fibrinogen, each sample being tested before use for its ability to form a stable clot with thrombin.[7] Cell and platelet free serum was tested for fibrinolytic activity, always within 24 hours of collection.

Twelve specimens of fresh menstrual "serum" have been examined. All contained marked fibrinolytic activity. A typical protocol is presented in Table 1. There was evidence that the enzyme was even more concentrated in the endometrial "debris" than in the "serum."[8]

During menstruation the venous serum of 5 women

[1] H. I. Glueck and I. A. Mirsky, *Am. Jour. Obst. and Gynec.*, 42: 267, 1941.

[2] E. L. Lozner, Z. I. Taylor and F. H. L. Taylor, *New Eng. Jour. Med.*, 226: 481, 1942.

[3] O. W. Smith and G. V. Smith, *Proc. Soc. Exp. Biol. and Med.*, 44: 100, 1940, and 55: 285, 1944.

[4] G. V. Smith and O. W. Smith, *Am. Jour. Obst. and Gynec.*, 45: 15, 1943.

[5] G. V. Smith and O. W. Smith, *Jour. Clin. Endocrinology*, 1: 470, 1941.

[6] H. J. Tagnon, C. S. Davidson and F. H. L. Taylor, *Jour. Clin. Invest.*, 21: 525, 1942.

[7] The thrombin employed was prepared by the Department of Physical Chemistry, Harvard Medical School, Boston, Mass., from blood collected by the American Red Cross, under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

[8] Since prothrombin is lacking in menstrual discharge,[1, 2] the formation of a clot when menstrual "serum" is added to oxalated plasma must be due to the formation of thrombin from the prothrombin of the oxalated plasma and the calcium of the "serum." No clot formed when washed endometrial "debris" was added to oxalated plasma unless calcium or thrombin was also added. Under the latter conditions the subsequent dissolution of the clot occurred with as little as 0.01 cc of "debris."

(10 specimens) was consistently fibrinolytic. A typical protocol is presented in Table 1. With 7 specimens from 4 of these women during the intermenstruum the tests were entirely negative. One woman, whose cycles are very irregular, had some of the enzyme in her serum on the 3 occasions during the intermenstruum when blood was taken, although fibrinolysis was minimal. Five other non-menstruating women gave negative tests, whereas the sera of 2 with abnormal uterine bleeding were fibrinolytic. Two specimens were tested 24 and 48 hours before the onset of flow. Both were positive.

TABLE 1

TYPICAL PROTOCOLS SHOWING THE FIBRINOLYTIC ACTIVITY OF SERUM

Material tested	cc*	Clot formation	Dissolution of clot†	Thrombin added at 1 hr.
Menstrual "serum"	0	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.1	None in 1 hour	.....	Clot (completely dissolved at 1 hr.)
	0.3	8 min.	Started at 15 min. +++ at 1 hr.	No clot
	0.8	5 min.	Started at 10 min. Complete at 1 hr.	No clot
Venous serum First day of menstration	0	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.1	None in 1 hour	.....	Clot (++ dissolved at 1 hr.)
	0.3	2 min.	Started at 30 min. ++ at 1 hr.	No clot
	0.8	1 min.	Started at 12 min. +++ at 1 hr.	No clot
Venous serum Severe preeclampsia at 8 months	0	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.1	20 min.	Started at 30 min. + at 1 hr.	No clot
	0.3	5 min.	Started at 15 min. ++ at 1 hr.	No clot
	0.8	1 min.	Started at 7 min. Complete at 1 hr.	No clot
Venous serum 24° after operation Pt.'s temp. = 100° F.	0	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.1	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.3	2 min.	Started at 8 min. ++ at 1 hr.	No clot
	0.8	1 min.	Started at 5 min. ++ at 1 hr.	No clot
A Typical Protocol from the Control Series				
Venous serum 9th day of a 31-day cycle	0	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.1	None in 1 hour	.....	Clot (none dissolved at 1 hr.)
	0.3	12 min.	None in 1 hr.	.....
	0.8	5 min.	None in 1 hr.	.....

* Each tube (13 × 100 mm) contained 0.2 cc of oxalated plasma and enough physiological saline to give a total volume of 1 cc when the serum was added. After incubation for one hour at 37.5° C., 10 + U of thrombin were added.

† Unless the clot was completely dissolved, the degree of dissolution was graded as follows: + = less than 0.5; ++ = 0.5 to 0.8; +++ = 0.8 or 0.9.

The sera from 7 patients with late pregnancy toxemia, one with eclampsia and one flowing prior to miscarriage at 4 months were tested. All 9 specimens were markedly positive for fibrinolytic activity. A typical protocol is presented in Table 1. The eclamptic patient and 2 of those with toxemia were studied 2 weeks later, when they had been delivered and were well. No enzyme was demonstrable. The sera of 7 normally pregnant women were also negative.

Although the enzyme and toxin are both concentrated in the euglobulin fraction of menstrual discharge, we have evidence that they are not identical. First, the fibrinolytic activity of many venous sera was as great as that in menstrual "serum"; whereas we have never been able to demonstrate toxicity in the venous serum of toxemic or menstruating women. Secondly, samples of menstrual discharge that have lost toxicity on standing may completely retain their fibrinolytic activity.

It has seemed to us that pathological syndromes associated with cellular injury from any cause whatsoever might be the effect of the release of toxic by-products of proteolysis from the action of this enzyme. To weigh this theory we have made preliminary studies on the blood of a few women before and after surgery. Of 8 patients taken at random, all with gynecological complaints, the sera of 4 contained fibrinolytic activity before operation. From the other 4, whose preoperative tests had been completely negative, bloods were taken one to 3 days after operation. All showed fibrinolysis. A typical protocol is given in Table 1. It is suggested that injured tissue produces a proteolytic enzyme.[9] This idea has also been recently expressed.[10]

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[9] In a recent paper (*Archives of Pathology*, 39: 28, 1945), V. Menkin refers to unpublished data indicating fibrinolytic action in the injury factor of canine pleural exudate. We have previously suggested[3] that his so-called "necrosin" and our menstrual "toxin" may be identical, both being products of cellular injury.

[10] A. Mirsky and E. D. Freis, *Proc. Soc. Exp. Biol. and Med.*, 57: 278, 1944.

SCIENTIFIC APPARATUS AND LABORATORY METHODS

PENICILLIN IN IODIZED OIL FOR INSTILLATION INTO THE LUNGS[1]

THE instillation of iodized oil as an aid in roentgen diagnosis of bronchiectasis, sinus tracts and other conditions is an established procedure. The addition of a potent anti-bacterial agent to the iodized oil might produce a valuable therapeutic aid in the above conditions.

The successful preparation and utilization of calcium penicillin in beeswax peanut oil[2, 3, 4] suggested the possibility of suspending penicillin in an iodized oil. It was necessary to establish the following facts: (1) that penicillin could be suspended in an iodized oil; (2) that iodized oil would have no adverse effect on the penicillin; (3) that the suspension would be stable, and (4) that the penicillin iodized oil would cause no damage to the tissues.

The penicillin iodized oil is prepared in the same manner as previously reported[2, 3, 4] for calcium penicillin beeswax peanut oil. Calcium penicillin is placed in a sterile mechanical blendor and a sufficient quantity of sterile 40 per cent. iodized oil is added. The mixture is blended for approximately 10 to 15 minutes. Each cc of the final suspension contains 1,500 Oxford units of penicillin per cc. The penicillin remains suspended in the mixture and does not settle.

Stability tests on the penicillin iodized oil indicate no adverse effect on the penicillin and show no deterioration when the mixture was kept at refrigerator, room and 37° C. temperatures for 60 days.

As initial experiments 8 rabbits were anesthetized and 1 to 3 cc of the penicillin iodized oil were injected through the trachea into the bronchi. Roentgen rays of the rabbits showed the penicillin iodized oil in the tracheobronchial tree. Depending on the amount of penicillin iodized oil instilled in the lungs, blood levels[5] of .039 to 1.25 Oxford units per cc were found at 15, 30 minutes, 1 and 2 hours. The rabbits were observed for a period of 2 months, at which time they were sacrificed. Gross and microscopic studies[6] of the lungs and other organs showed no abnormalities as a result of the instillation of the penicillin iodized oil into the lungs.

The practicability of treatment of pulmonary suppurative processes by the local application of penicillin iodized oil was suggested by the rabbit experiments. Ten patients with severe saccular bronchiectasis and two with pulmonary abscess were selected. The lesions in all 12 cases were confined to one lobe of the lung.

After preliminary cocainization of the posterior pharynx the supra-glottic inhalation method was employed to introduce 7 to 10 cc of the penicillin iodized oil into the diseased pulmonary lobe. Positioning of the patient with fluoroscopic visualization of the iodized oil furnished an accurate check concerning the location of the material.

No immediate or subsequent discomfort due to the mixture was observed. Although only occasional assayable levels of penicillin were found in the bloods which were taken at 15, 30 minutes and 1, 2 and 3 hours after the single instillation of the penicillin iodized oil, penicillin continued to be excreted in the urine for at least 24 hours in all patients.

Of the 12 patients who had a single bronchial instillation of the penicillin iodized oil, 2 of the cases, one bronchiectasis and the other lung abscess, had a gradual reduction in sputum by the seventh day to approximately 50 per cent. of the original amount. By the end of a two-week period, the sputum output in both cases had returned to the amount prior to treatment. In the remaining ten cases, no significant changes were noted.

It is apparent that no definite conclusions can be drawn from the clinical studies which have been discussed. The chances of curing far advanced bronchiectasis, lung abscesses or any type of chronic pulmonary suppuration by this method seem unlikely. There is, however, a distinct possibility that the bacterial flora in the diseased lungs may be altered and make subsequent surgical intervention safer. Penicillin iodized oil may also be of value as a palliative treatment in subjects who are unsuitable risks for radical treatment.

COMMENT

Others[7, 8] have previously shown that Penicillin Aerosol penetrates the lung and may be recovered from the urine. However, by this method it is neces-

[1] From the Penicillin Section, Laboratory Service and the Thoracic Surgery Section, Walter Reed General Hospital. The technical assistance of Miss Dorothy Talbot and Technician (4th Grade) Minna Levy is gratefully acknowledged.

[2] M. J. Romansky and G. E. Rittman, SCIENCE, 199: 196, September 1, 1944.

[3] M. J. Romansky and G. E. Rittman, *Bull. U. S. Army Med. Dept.*, October, 1944, p. 43.

[4] M. J. Romansky, R. J. Murphy and G. E. Rittman, *Jour. Am. Med. Asn.*, June 9, 1945, pp. 404–407.

[5] Assays of penicillin in the blood, urine and for stability were done by the methods of Rammelkamp, *Proc. Soc. Exp. Biol. and Med.*, 51: 95–97, October, 1942; G. Rake and H. Jones, *Proc. Soc. Exp. Biol. and Med.*, 54: 189, November, 1943; and W. M. M. Kirby and L. A. Rantz, *Jour. Bact.*, 48: 603, 1944.

[6] 1st Lt. Ellery M. James, pathologist at Walter Reed General Hospital, examined the sections.

[7] V. Bryson, E. Sansome and S. Laskin, SCIENCE, 100: 33–35, 1944.

[8] A. L. Barach, F. H. Silberstein, E. T. Oppenheimer, T. Hunter and M. Soroka, *Annals of Int. Med.*, 22: 485, 1945.

sary to give inhalations, as many as four to five times daily, to maintain satisfactory quantities of penicillin in the lungs. Moreover, when Penicillin Aerosol is employed radiographic control of the location of the agent is not possible.

The primary purpose of this study has been to illustrate that after a single instillation of penicillin iodized oil, penicillin is present locally in the lungs for a minimum of 24 hours, as indicated by its excretion in the urine for that period of time. Further study is necessary relative to the frequency and interval of instillation of penicillin iodized oil as well as the therapeutic possibilities.

SUMMARY

(1) A suspension of calcium penicillin in 40 per cent. iodized oil produces a stable mixture which has been instilled in the lungs of 12 patients without adverse effect and has maintained penicillin in the lung for a minimum of 24 hours, after a single instillation.

(2) The penicillin iodized oil has maintained its potency for 60 days at ice box, room and 37° C. temperatures.

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CHROMOSOME MOUNTS FOR TEMPORARY STUDY

ZIRKLE'S[1] solution, or a modification of this, as a sealing agent for the temporary preservation of chromosome mounts has been found to be more effective and more convenient than any of the various paraffin or wax and gum mastic mixtures. With a pipette a small amount of Zirkle's solution—80 cc aceto-carmine, 10 cc Karo corn syrup (Dextrose), and 10 cc Certo (Pectin)—is placed around the edges of the cover slip and allowed to dry. By this method smears of leaves,[2] root tips and anthers have been preserved in good condition for periods varying from several weeks to several months. The procedure is equally effective with propio-carmine, Feulgen, and aceto-carmine smears.

The solution has been modified by substituting 45 per cent. acetic acid for the aceto-carmine and the resulting solution used as a sealing agent. While slides so sealed do not seem to remain in good condition as long as those prepared by the first method, excellent results have been obtained with slides kept for periods up to a week or ten days. Since the possibility of over-staining which might result from the presence of Zirkle's solution around the edges of the cover slip is thereby avoided, this modified solution is suggested for slides which are to be kept for short periods.

In addition to the effectiveness of these solutions as sealing agents and the ease with which they are applied, they are also recommended, for slides sealed by them can be made into permanent mounts by removing the solution from the edges of the cover slip with a moistened cloth, by inverting the slide in acetic alcohol (1:1) until the cover slip floats off, and by following from here Meyer's[3] procedure for making smears permanent, or by using any desirable modification of McClintock's[4] permanent aceto-carmine method.

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DISCUSSION

THE LAPLACE EQUATION

THE most important partial differential equation is

$$\frac{\partial^2\phi}{\partial x^2}+\frac{\partial^2\phi}{\partial y^2}=0, \tag{1}$$

known as the Laplace equation. The applications embrace gravitation, electricity, magnetism, hydrodynamics, conduction of heat, stream lines, isothermal families, conformal mapping.

In three dimensions, the corresponding equation is

$$\frac{\partial^2\phi}{\partial x^2}+\frac{\partial^2\phi}{\partial y^2}+\frac{\partial^2\phi}{\partial z^2}=0. \tag{2}$$

This equation is much more complicated analytically; in particular the powerful method of functions of a complex variable successful for (1) is no longer available for (2).

Although the analytic difficulties are well known, we shall point out new geometric aspects. Sophus Lie found the first geometric property of isothermal families of curves in the plane. We prove that this result is no longer valid in three dimensions. From Lie's work, Kasner and De Cicco found purely intrinsic geometric properties of isothermal families and isothermal networks. These have applications to stream lines in two dimensions.

Our object is to find analogues in three dimensions.

[1] C. Zirkle, SCIENCE, 85: 528, 1937.
[2] J. T. Baldwin, Jr., SCIENCE, 90: 240, 1939.
[3] James R. Meyer, *Stain Tech.*, 18: 53–56, 1943.
[4] B. McClintock, *Stain Tech.*, 4: 53–56, 1929.

The discussion is very complicated and not complete, but we report progress. Lie's theorem refers to the single inclination of the curve; but in space we have to introduce two slopes, or three direction angles of the surface. We find that these slopes or angles obey a fundamental set of three partial differential equations of second order. (In Lie's case, he found a single equation of second order which was identical in form with Laplace's equation). Our new equations are not of the Laplace form.

It is well known that the only transformations which convert (1) into itself form the conformal group. This is obvious from the theory of functions of a complex variable. Therefore isothermal families are converted into isothermal families by conformal transformations. The authors have proved that no other point transformations are legitimate. This is difficult because we can no longer take advantage of the isothermal parameter, and therefore we have to use an equation of third order, related to the Laplace equation, but not identical with it.

Now in three dimensions it is shown that the only legitimate point transformations which send (2) into itself are those of the similitude seven-parameter group. Thus we have merely arbitrary constants but no arbitrary functions. For isothermal families of surfaces, our discussion yields the same group.

If, instead of point transformations, we use the larger body of contact transformations, no new auto-transformations are possible. However, by using general element transformations, we have discovered a larger set of possibilities in the plane. Studying the analogous situation in space, we prove that no larger group can exist.

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THE RATE OF DEVELOPMENT OF RED CELL PRECURSORS

SEVERAL attempts have recently been made to answer the question as to whether there are sufficient cells in the early developmental categories to maintain the number of mature red cells in the circulating blood. The solution of the general problem is simple when one approaches it from the standpoint of the steady state, and in the adult rat there are figures of sufficient accuracy to enable one to carry out the calculations.

Assuming that the cells of the red cell series develop irreversibly from hemocytoblasts to mature erythrocytes by passing through the successive stages of erythroblast, normoblast and reticulocyte, the number of cells N in any one class per unit volume at any one time will depend on P, the number of cells which enter the class per unit time, and Q, the number which leave it in unit time to enter the next class of the consecutive development. In the steady state in which N for the class remains constant, being fed by cells from the class before it as it delivers cells into the class beyond it,

$$t = N/Q,$$

where t is the average duration of the life of the cell in the class. When there is no cell division, $P = Q$, and the P for any class is the Q for the class before it.[1] If some of the cells in the class undergo mitotic division, the fractional number of cells which divide is

$$f = mt/d$$

where m is the number of the cells in the class observed in mitosis at any one time and expressed as a fraction of unity, and d is the duration of a mitosis in the same units of time as used to express t. For such a class in which a fraction of the cells divide, P is smaller than Q, and is

$$P = Q(1 - f/2).$$

The values assumed for the adult rat are shown in Table 1.

TABLE 1

Class	N per mm³	Explanation
Mature red cell	18.8×10^6	$9.0 \times 10^6 \times 6.27/3.02$*
Reticulocyte	11.6×10^6	$5.4 \times 10^6 \times 6.27/3.02$
Normoblast	7.2×10^5	36 p.c. of 2×10^6†
Erythroblast	8.0×10^4	4 p.c. of 2×10^6
Hemocytoblast	5.0×10^4	2.5 p.c. of 2×10^6; 50 p.c. of all hemocytoblasts present.

* Ratio of circulating blood to active marrow, Fairman and Corner.[7] The multiplication makes 1 mm³ of marrow equivalent to 1 mm³ of blood.
† Total number of cells per mm³ of marrow, Kindred,[5] Farrar.[8]

Starting the calculations with $t = 60$ days for the mature red cell, and assuming (a) that the fraction of cells observed in mitosis in the normoblast, erythroblast and hemocytoblast classes is $m = 0.005$,[2] and (b) that d is 0.5 hour, we get the values shown in Table 2.

The number of cells which must be produced by the cells of the erythrogenic capillaries or other cells of origin in order to maintain the steady state is accordingly 2.12×10^5 per mm³ of marrow per day. This is not a remarkable rate of production; if, for

[1] E. Ponder, *Quart. Jour. Exp. Physiol.*, 16: 241, 1926.
[2] Kindred,[5] Table 2. The value 0.005 is applied to all three classes as an approximation, but the number of mitoses is small, and even considerable variation in the value would not affect the final result much. No account is taken of amitotic divisions.

TABLE 2

Class	t, days	Q, per mm³./ day	P, per mm³./ day	f
Mature red cell	60	3.13×10^5	3.13×10^5	0
Reticulocyte	3.6	3.13×10^5	3.13×10^5	0
Normoblast	2.3	3.13×10^5	2.27×10^5	0.55
Erythroblast	0.35	2.27×10^5	2.18×10^5	0.084
Hemocytoblast	0.23	2.18×10^5	2.12×10^5	0.055

example, the cells of the erythrogenic tissue were 5 per cent. of the total number in the marrow, only 2 mitoses per cell per day would be required. Whether or not this development occurs in erythrogenic capillaries involves the recognition at any one time of the presence (Sabin[3]), or absence (Jordan,[4] Kindred[5]), of cell division in about one capillary endothelial cell out of 25. Such a marrow would regenerate from the depleted state in about 10 days. The difficulty which Jordan, Kindred, Duran-Jorda[6] and other investigators have experienced in finding a sufficient number of precursors to maintain the red cell population in the steady state is thus considerably reduced when the precursors are regarded as *becoming* the cells of the subsequent classes by maturation instead of as *giving rise* to the cells of subsequent classes by mitosis; it should be understood, however, that my purpose is not to try to settle the question, but to call attention to this way of approaching the problem.

The same type of calculation is applicable to the steady state of the granulocytes, but here the difficulty is to assign a value to N for the class of the polymorph, because this cell is present not only intravascularly but also extravascularly. Reasonable values, however, point to the duration of life of the various white cell precursors being longer than that of the red cell precursors.

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FLUORESCENT MICROSCOPIC STUDY OF THE PHYSIOLOGICAL DISTRIBUTION OF ATABRINE

STUDY of the pharmacology of atabrine has led to a more rational use of the drug and increased its efficiency as an anti-malarial agent. Chemical determinations have demonstrated that atabrine is localized chiefly in leucocytes, liver, spleen and kidney.[1] The study here reported has been undertaken to determine where, within the tissues, atabrine is localized, in an attempt to better understand its action on the infectious organism.

The fluorescent property of atabrine, with its maximum wave-length at 365 mμ, is utilized in its chemical determination in plasma.[2,3] The same principle is used in the microscopic study. The source of illumination is from an H-4 bulb mounted in an ordinary microscope lamp attached to the appropriate transformer. A Corning No. 5984 filter is interposed in front of the lamp and a Corning No. 3894 filter, ground down to fit the ocular, is used as the selective filter.

Fluorescent microscopy has been utilized for some time. Dempsey[4] and Dempsey and Wislocki[5] have recently used it extensively. However, these authors use ultra-violet light and quartz lenses throughout and therefore could detect true fluorescence of tissue. The fluorescence used in this study is at a wave-length of 365 mμ, which is within the range of visible light, and therefore glass lenses can be used.

Frozen sections are made from fresh tissue, or after fixation in neutral or slightly alkaline formalin, and mounted in saline or 0.2 M Na_2HPO_4. (Atabrine shows its greatest fluorescence at pH 9.5 in aqueous solutions.) No method has been perfected for making permanent mounts of these sections. The above technique is a modification of the method of Popper.[6]

Adult male and female mice were injected intraperitoneally with a 2 per cent. solution of atabrine hydrochloride, the daily dosage being 2 mg and the total dosage 4–12 mg. Uninjected mice were sacrificed and studied simultaneously with each test animal. Control tissue shows a slight amount of yellowish fluorescence which is diffuse throughout the entire section, although under the high power (440X) it is barely visible. However, the fluorescence of atabrine is of an entirely different color, being yellowish green, and has an intensity so much greater that the diffuse yellowish background is completely lost. With this method the absence of fluorescence manifests itself as a black background.

Preliminary studies revealed the greatest concentration in the liver, spleen and kidney, as has been demonstrated quantitatively by Shannon *et al.* In the liver fluorescence appeared diffusely distributed throughout the parenchymal cells. The nuclei showed no greater concentration than the cytoplasm. The sinusoids appeared black and there was no evidence of any great concentration within the Küpffer cells. In the spleen, the fluorescence appeared to be con-

[3] F. R. Sabin, *Physiol. Reviews*, 8: 191, 1928.
[4] H. E. Jordan, *Anat. Record*, 73: 227, 1939.
[5] J. E. Kindred, *Amer. Jour. Anat.*, 70–71: 207, 1942.
[6] F. Duran-Jorda, *Lancet*, 186, Aug. 14, 1943.
[7] E. Fairman and G. W. Corner, *Anat. Record*, 60: 1, 1934.
[8] G. E. Farrar, *Amer. Jour. Physiol.*, 117: 662, 1936.
[1] J. A. Shannon, *et al.*, *Jour. Pharm. and Exp. Therap.*, 81: 307, 1944.
[2] B. B. Brodie and S. Udenfriend, *Jour. Biol. Chem.*, 151: 299, 1943.
[3] J. M. Masen, *Jour. Biol. Chem.*, 148: 529, 1943.
[4] E. W. Dempsey, *Endocrin.*, 34: 27, 1944.
[5] E. W. Dempsey and G. B. Wislocki, *Endocrin.*, 35: 409, 1944.
[6] H. Popper, *Arch. Path.*, 31: 766, 1941.

centrated within the Malpighian corpuscles and there was very little within the sinusoids. This would suggest that high concentrations of atabrine were not attained within the reticulo-endothelial cells. In the kidney the convoluted tubules showed the greatest fluorescence, the collecting tubules a lesser amount, and the glomeruli but little. Fluorescence in other organs was not as great as in the three organs first described.

Further, it is not yet definitely established that this is all due to atabrine alone because no distinction can be made between atabrine and its degradation products by this technique.

JOSEPH W. JAILER,
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THE EFFECT OF MOTION PICTURES ON BODY TEMPERATURE

THE letter from Mr. N. Kleitman in SCIENCE for May 18 on "The Effect of Motion Pictures on Body Temperature" is of interest, in that it gives an apparent anomaly.

Although I am not a biologist, there would appear to be two possible complicating factors of which no mention is made, and it would be interesting to know whether there is any correlation in respect of these two points.

(1) It would be expected that the type of film would have an overwhelming effect on any rise in body temperature. It seems unreasonable to suppose, among the wide variety of films seen by habitués, that a similar rise in body temperature would be occasioned by widely different types of film; the figures show a similar rise in body temperature for all types of film, and one feels from this that some other factor may well be involved. The point is well put that a film need not necessarily be a relaxation and it can, of course, give rise to intense emotions, but it would have been thought that in the case of a habitué, many films would certainly not have a very intense effect. I myself go rarely, but there appear to be a good proportion of very disappointing feature films which should affect the figures given.

(2) A possible overriding factor may be the rise in body temperature occasioned by close contact with masses of other people in a confined space. The normal diurnal temperature drop expected at the time when the habitué went to the cinema presumably occurs in conditions of uncrowded living at home. I am not sufficiently familiar with the American conditions to know if it is a reasonable assumption that the average temperature in the home of the habitué would be reasonably lower than the temperature in the cinema, but in any case, proximity to considerable numbers of other human beings is likely to have an appreciable effect on temperature.

It would be interesting to know whether any data have been taken for, say, rise in body temperature at a concert or something less stimulating, or possibly a soporific election meeting, if such are held in America.

R. BARRINGTON BROCK

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SUGGESTION FOR THE DISCHARGE OF SCIENTISTS FROM THE ARMED FORCES

RECENT discussion in scientific circles and journals points out that the United States faces a serious decline in the progress of scientific research for a period at least equal to the "duration," since it has placed its younger scientists of draft age in active service. Concern over this matter has been most expressed in the field of medicine and in the physical sciences because of their practical importance. The same concern should be felt and voiced with respect to those fields of pure science in which immediate importance is not evident. The several sciences interlock so completely that in the long run it is as disastrous to interrupt a train of thought dealing with quaternions or to take a research anatomist away from the study of the giant panda as it is to halt research on poison gases or their antidotes, or on stratospheric trajectories.

That the so-called pure sciences form the framework of all scientific research is so evident that we should now look from the immediate bearing to the remote bearing of our allocation of scientific personnel. A proper coverage of the sciences in the organization of our American scientific personnel becomes the more important when it is remembered that with an impoverished or ruined Europe America must shoulder a much greater share of the cultivation of the sciences than ever before.

Since, however, the temper of the country at large and likewise the temper of our most promising young scientists seem to be definitely against any general deferment of such a group of young men, however great their future importance to science and to the nation, we seem to be at an *impasse*. Finding no solution to the problem as a whole, I venture a suggestion for a segment that seems solvable. This lies in the discharge of all men now in the armed forces who are past the age of 30, below the commissioned rank and for whom a research position in a university, museum or research institute is being held open. A man below the officer rank, and past the age of 30, who holds a responsible research position in a scientific institution would obviously serve the national interest better if returned to his civilian scientific post. The performance of the tour of duty indicated by his age will remove any feeling on the man's own part (or in that of his fellows) that he has shirked a na-

tional duty. The fact that he is not a commissioned officer will indicate that his training as a scientist is not of primary importance to the army. The fact that a position is waiting for him means that his discharge would contribute to orderly demobilization. Postwar expansion of the national scientific program will require the aid of exactly the age group in question as teachers and leaders.

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SCIENTIFIC BOOKS

CLINICAL MYCOLOGY

Manual of Clinical Mycology. Prepared under the auspices of the Division of Medical Sciences of the National Research Council. 348 pp. Philadelphia and London: W. B. Saunders Company. 1945.

THIS war manual is useful for the general practitioner, as well as for the clinical pathologist. We can accept the mycologic nomenclature and taxonomy of Dr. Conant with complete confidence. The medical authors have cooperated to produce a volume that is practical and scientific from the point of view of the pathologist as well as the dermatologist.

Surgeon General Kirk, in his "Foreword," recognizing the need for such a book, has stated, "In many places in this country medical mycology is a field of esoteric interest." Probably the best definition of esoteric is understood by the initiated alone.

Surgeon General McIntire states that the book is to be highly recommended for its timeliness and soberness of presentation, and that "Treatment is definitive and modern."

In the first edition of my little manual of clinical pathology (1908) I had the advice of our great parasitologist, Dr. Charles W. Stiles, but for mycology I was at a loss for guidance. Fortunately, I found a book which, I felt, was authoritative, written by L. Gedoelst, and published in Brussels, in 1902. Since then I have also been guided by Vuillemin and Brumpt. One reason for my preference for French parasitologists has been that Dr. Stiles considered the French far superior to the Germans in accuracy of nomenclature. Dr. Stiles was for many years the secretary of the International Committee on Zoological Nomenclature.

In the last edition of my book, at the recommendation of Dr. Thom, I turned to the splendid work of Professor Dodge ("Medical Mycology"). Dr. Stiles regarded our American nomenclaturists as on a par with the French.

In the excellent chapter on Cryptococcosis the name of the fungus is given as *Cryptococcus neoformans.* I have discussed this most serious and important invader of the central nervous system under the name of *Cryptococcus histolyticus* (*Torula histolytica*), and designating the disease as torulosis. It is evident I shall have again to consult my mycology friends.

The chapters on Coccidioidomycosis, South American Blastomycosis, Chromoblastomycosis and Histoplasmosis give us detailed, easily understood and recent information as to these diseases.

The bibliography is of great aid to teachers of mycology. The illustrations are well chosen.

Vice Admiral McIntire importantly states, "Our tropical warfare, particularly in the bush jungles of the South Pacific, has fostered fungus growth to a crippling degree."

There is an editorial in *The British Medical Journal* of May 13, 1944, which states, in connection with reconversion postwar changes in medical education: "Most of the text-books of the present must go on the reference book shelf, where they properly belong, and new text-books must be written and practical courses prepared, directed to study of method and principle."

This little war manual, prepared by staff members of the Duke University School of Medicine, including a pathologist, a dermatologist, an internist and a trained mycologist, submitted their manuscripts to Dr. Martin, who coordinated the various sections to make the style more uniform.

This would seem to be the type of book the British had in mind.

Since the preparation of this manual of mycology a very disturbing piece of research work by the Tuberculosis Control Division of the Public Health Service has appeared (Carrol E. Palmer, May 11, 1945). This deals with nontuberculous pulmonary calcifications and sensitivity to histoplasmin. This throws doubt on the validity of chest plates used as a basis for rejecting persons for the armed services.

Epidemiological surveys were made in widely separated areas of the United States, and striking variations were obtained as to percentage of histoplasmin reactors. Data as to tuberculin and histoplasmin tests with roentgenograms on 3,105 student nurses were studied.

The greatest incidence of such pulmonary calcifications, in nurses showing histoplasmin reactions, was found in Kansas City, Mo. (61.5 per cent.)—in Philadelphia, Pa., only 11.8 per cent.

The histoplasmin was supplied by Dr. C. W. Emmons, of the National Institute of Health.

Earlier reports were made by Olson, Wright and Nolan, of the U. S. Public Health Service, as to the nature of pulmonary calcifications in those not showing clinical or tuberculin-test evidence of tuberculosis.

Interesting to zoologists, is the research work as to the possibility that these nontuberculous pulmonary calcifications might be connected with *Ascaris* larvae passing through the lungs. It was concluded that the epidemiological study did not prove or disprove the possible rôle of *Ascaris*.

In talking with Dr. Emmons, he took a conservative view as to definitely incriminating *Histoplasma capsulatum*, notwithstanding the frequency of positive histoplasmin reactions, as contrasted with coccidioidin ones.

Following World War I there were many cases of infection with *Coccidioides immitis* reported from California, and the burden of evidence indicated a fatal termination.

As noted in this war manual it is now recognized that there are types of coccidiomycosis which are relatively benign, with cases reported from Texas, Arizona and New Mexico. In Arizona from 75 to 97 per cent. of Indian children reacted positively to coccidioidin. Positive coccidioidin tests were essentially negative among the nurses except for nurses who had lived in California or southwestern parts of the United States.

Histoplasmosis too had been formerly considered as a fatal infection.

I heartily recommend this timely and authoritative war manual to clinical pathologists.

E. R. STITT,
Surgeon General, U. S. Navy, retired

DAIRY CATTLE BREEDING

Heredity in Dairy Cattle. By JAMES E. RUSSELL. 135 pp. Illustrated. The American Guernsey Cattle Club, Peterborough, New Hampshire. 1944. $2.50.

THIS book by James E. Russell, formerly dean of Teachers College, Columbia University, and for many years a breeder of Guernsey cattle, is intended as a guide and inspiration for the successful business man and young person considering the breeding of cattle either as a vocation or avocation. It is not, as its title might imply, a scientific treatise on inheritance in cattle.

In his preface the author pays tribute to the scientific workers who have discovered the underlying principles of inheritance, but says that Part I is to treat of the "few important biological principles which have a direct bearing on the breeding of dairy cattle . . . and not to be greatly concerned with the methods of scientific procedure or the successive stages by which reliability of findings has been established . . . we stress the action of genes rather than the behavior of chromosomes . . . and will avoid concise technical terms like gamete, heterozygote, etc." Part II is to be the story of some successful breeders and a cattle family. Part III, personal experiences.

Part I, Theory of Genetics, while generally in keeping with present knowledge of inheritance, contains many loose and ambiguous statements of which the following are examples:

In effect, only *one-fourth of the possible combinations of chromosomes* in the two original sex cells which unite in the fertilization of an egg cell do appear in the resulting new individual. . . .

The necessity of getting rid of half the chromosomes in maturing sex cells in order that the standard number of the species be restored at the time of conception raises questions of special interest to breeders. Is it merely a matter of chance that decides what each offspring of a particular pair gets? *May it happen that one member of a family gets more from one parent than do brothers or sisters? Or, in an extreme case, may one offspring get its inheritance solely or largely from one parent and little or nothing from the others?* . . .

We know now that nothing except external physical injury can disturb the normal development of an unborn child. . . .

In animal breeding there is no escape from the necessity of dealing with a "mixed lot." However, Mendel pointed out that each character operates as a unit and that whenever two are opposed, one becomes dominant and the other recessive while biding its chance to appear again.

The author's attempt to popularize the genetics of cattle is on the whole not too successful, although he has made it interesting and woven a lot of his own philosophy of life into it. The halving and sampling nature of the hereditary process, for example, is nowhere made clear.

Part II deals with the art of breeding and for illustrative material the author discusses a successful small herd, a large commercial herd, his own herd and the Mixter Faithful strain of Guernseys.

The small herd and farm is that owned by Vernon D. Mudgett at Sterling Junction, Massachusetts. Mr. Russell has woven an interesting and inspiring story of Mr. Mudgett's accomplishments. Taking over an old somewhat run-down farm when just out of college, Mr. Mudgett, with a cash start of only $1,000, has developed a very profitable farm business and one of the best small Guernsey herds in the East. By hard work; careful planning; being ever ready to learn and to try out new methods; by making old things do until cash was available to provide the new; and last but far from least, by choosing the proper sort of girl for his wife and helpmate Mr. Mudgett has, relatively early in life, established himself as one of the leading farmers and breeders in his state.

Mr. Russell correctly stresses the advantages of diversification for the small farmer using Mr. Mudgett's experiences with poultry, fruit, milk and

breeding stock to drive his point home. The best part of the story from this reviewer's standpoint, is that relating to Mr. Mudgett's progress in breeding a splendid herd of Guernseys from 3 or 4 well-chosen foundation cows coupled with his carefully studied plan of choosing sires. In the latter is exemplified the wisdom of choosing sons of proved sires out of daughters of proved sires—said daughters also being members of good cow families. The breeding story would have been more easily followed had Mr. Russell made a family chart of the whole herd rather than using narrative and tables and had he included some pedigrees.

The large commercial dairy herd discussed is the Overbrook herd in Essex County, New Jersey. Management of this Holstein herd was assumed by Mark H. Keeney in 1923. This astute manager and breeder set as his goal a large herd that would average over 500 pounds of butterfat per cow per year and not only reached his goal but has held it over 10 years. In a herd numbering 70 to 80 cows this is a truly remarkable accomplishment. Mr. Keeney, in his own book, "Cowphilosophy," has told the story in detail. Mr. Russell in his discussion dwells largely on Mr. Keeney's choice of sires which follows the pattern already described in the small Guernsey herd of Mr. Mudgett.

In writing about his own herd, Mr. Russell says, "Four or five generations on bovine history—weaken the memory," and, of course, he might very well have added, "also the genetic influence." Mr. Russell has apparently done a splendid job of breeding Guernseys, but his telling about it would have been more clear had he used a herd chart and included some pedigrees. When several hours of work had put Mr. Russell's words into the form of a herd chart and we had traced several pedigrees, we learn that his foundation cow made 654 pounds of butterfat; 3 daughters averaged 675 pounds; 10 granddaughters averaged 697 pounds; 17 great granddaughters averaged 704 pounds and 5 great, great granddaughters 717 pounds. This is a great cow family.

Also from the chart, we can see that the first bull's daughters averaged 633 pounds of fat; the second bull's 9 daughters—688 pounds; the third, 8 daughters—689 pounds; the fourth, 4 daughters—730 pounds; the fifth, 3 daughters—737 pounds; the sixth, 4 daughters—756 pounds; the eighth, 2 daughters—681 pounds.

These are selected advanced registry records of the cows in this cow family. What all the daughters of this succession of bulls averaged and how the daughters' average compared with that of their dams, we do not know. To make progress in breeding we need all the facts—not the few selected best ones.

The chart of this cow family also reveals that there are great differences among the different lines within the family.

Part II concludes with a discussion of the Mixter Faithful strain of Guernseys and again the lack of pedigrees makes the material hard to visualize and retain.

Part III, a short essay titled "Personal Experiences and Suggestions," is utilized by Mr. Russell to sum up Parts I and II for those who may be thinking of embarking on a cattle breeding enterprise and to philosophize on farming and breeding both as a way of life and of making a living.

In this last section, as indeed throughout the book, the author seeks to warn the unwary of the seemingly devious ways of nature in failing to live up to the old adage that "like begets like" but he does not attempt an elucidation of the genetic and environmental causes of variation.

In the writer's opinion the book should be stimulating to animal lovers of all ages. His main criticisms are (1) that the author is inclined to play a little fast and loose with the science of genetics for the sake of popularization, thereby failing to make genetic principles stand out as clearly as they might have been made to do; and (2) that, since the author knew Guernsey history and pedigrees so thoroughly himself, he did not deem it wise to use more pedigrees and family charts relying alternatively on narrative and thus making reading and retention more difficult for the average reader.

V. A. RICE

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